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ORIGINAL CONTRIBUTIONS

- MEDICAL TREATMENT OF CARDIOSPASM—*H. Necheles, M. D., H. Laski, M. D., L. D. Elegant, M. D. and R. Baum, M. D.* 121
- COMPLETE NON-ROTATION OF THE GUT AND TORSION OBSTRUCTION OF THE COLON IN AN ADULT—*W. P. Kleitsch, M. D. and H. G. Reiser, M. D.* 123
- GASTROSCOPIC EXPERIENCES IN THE UNITED STATES ARMY, EUROPE—*Col. Robert S. Nelson, M. C.* 128
- STUDIES OF AEROGENIC AND ANAEROGENIC VARIANTS OF *SALMONELLA SCHOTTMUELLERI*. II. RESISTANCE TO ANTIBIOTICS AND SULFADIAZINE—*Charles Gainor, Ph. D. and William O. Weigle, M. S.* 133
- GANGRENOUS CHOLECYSTITIS RESULTING IN DEFECT OF THE HEPATIC DUCT: SUBSEQUENT HYPERSPLENISM—*A. Strelinger, M. D.* 136
- EVALUATION OF A NEW METHOD FOR SUPPLEMENTATION OF GASTRIC HYDROCHLORIC ACID—*George S. Sharp, M. D. and John W. Hazlet, D. D. S.* 140

ABSTRACTS ON NUTRITION, EDITORIAL, BOOK
REVIEWS, GENERAL ABSTRACTS OF CURRENT
LITERATURE 144-148

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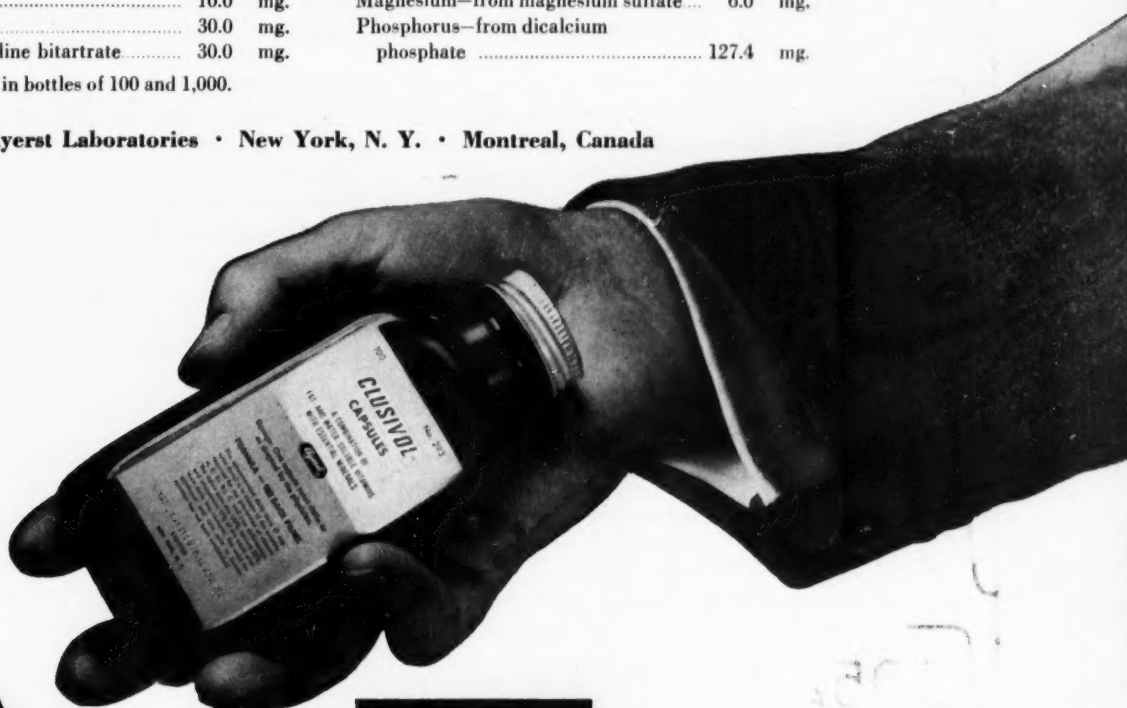
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Best, R. R.; Hicken, N. F., and Finlayson, A. I.: *Ann. Surg.* 110:67, 1939.

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Cranshaw, J. F.: *Am. J. Digest. Dis.* 17:387, 1950.

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Beckman, H.: *Pharmacology in Clinical Practice*, Philadelphia, W. B. Saunders Company, 1952, p. 361.

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O'Brien, G. F., and Schweitzer, I. L.: *M. Clin. North America* 37:155 (Jan.) 1953.

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Water	50%	50%	59%	60%
Protein	21 Gm.	20 Gm.	27 Gm.	25 Gm.
Fat (ether extract)	28 Gm.	20 Gm.	13 Gm.	13 Gm.
Niacin	4.0 mg.	4.3 mg.	5.5 mg.	4.2 mg.
Riboflavin	0.21 mg.	0.19 mg.	0.22 mg.	0.23 mg.
Thiamine	0.46 mg.	0.40 mg.	0.08 mg.	0.02 mg.

*Values after conversion from 42% to 50% water basis.

**Values after conversion from 58.69% to 50% water basis.

Experimental studies have shown that the processing which meats-in-a-can undergo leads to little if any greater vitamin losses than does home-cooking of similar cuts of meat. In general, meats-in-a-can retain of their original vitamin content approximately:

- 60 to 80 per cent of thiamine
- 90 to 100 per cent of riboflavin
- 90 to 100 per cent of niacin
- 80 per cent of biotin
- 70 to 80 per cent of pantothenic acid.^{4,5}

During storage for customary periods, at usual warehouse temperatures, meats-in-a-can show little, if any, further vitamin loss except in thiamine. Even thiamine, a highly thermolabile vitamin, was 52 per

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1. Howe, P. E.: *Foods of Animal Origin*, Handbook of Nutrition, American Medical Association, ed. 2, Philadelphia, The Blakiston Company, 1951, p. 637.

2. Watt, B. K., and Merrill, A. L.: *Agricultural Handbook No. 8*, United States Department of Agriculture, 1950.

3. Schweigert, B. S.; Bennett, B. A.; Marquette, M.; Scheid, H. E., and McBride, B. H.: *Food Res.* 17:56 (Jan.) 1952.

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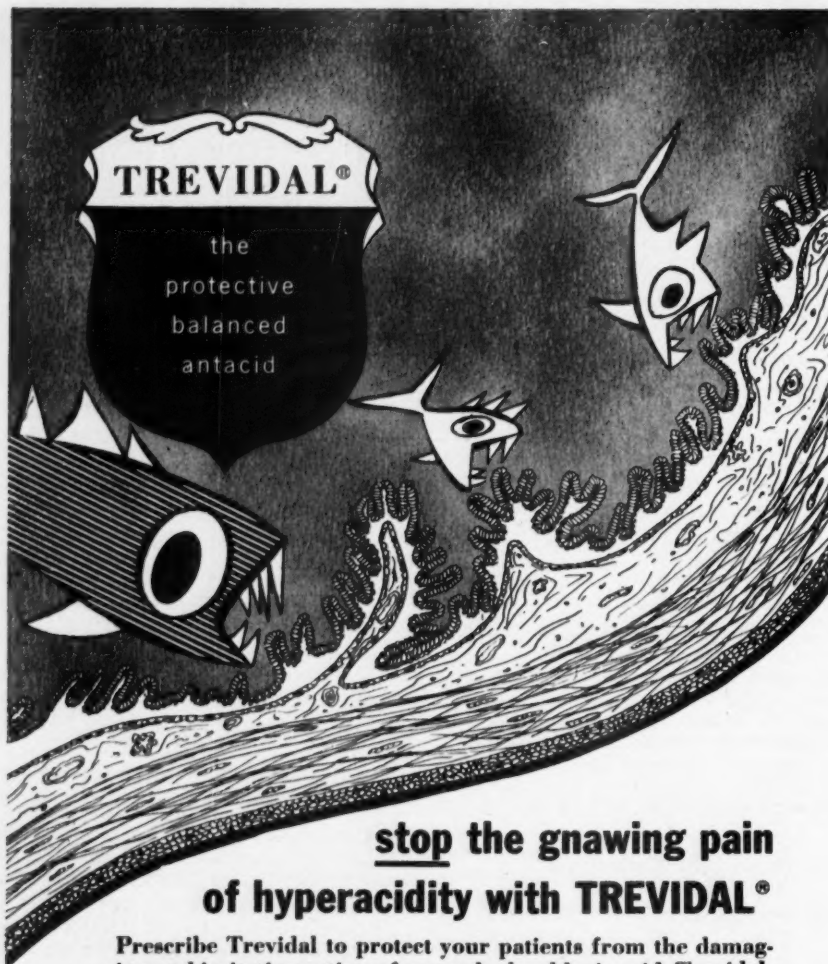
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6. Schweigert, B. S.; Bennett, B. A.; McBride, B. H., and Guthneck, B. T.: *J. Am. Dietet. A.* 28:23 (Jan.) 1952.

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MEDICAL TREATMENT OF CARDIOSPASM

H. NECHELES, M. D., PH. D., H. LASKI, M. D., L. D. ELEGANT, M. D., AND R. BAUM, M. D.,* Chicago, Ill.

THE ETIOLOGY of cardiospasm can be classified into two main categories, namely, external and internal factors. External factors would be disturbances from sources extraneous to esophagus and cardia, causing cardiospasm by reflex. Internal factors would consist of disturbances in the esophagus and cardia and their innervation (achalasia).

Achalasia of the cardia has been assumed to be due to loss of intrinsic cholinergic ganglion cells in the region of the cardia. These ganglionic plexuses would, under normal conditions, relax the sphincter, and prevailing adrenergic impulses would keep the sphincter closed (1). Recently, the evidence of cardiospasm as a local nervous disturbance of the cardia has been weakened by observations of generalized disturbances in the entire esophagus (2-4), and by the finding that a powerful sympatholytic drug, dibenamine, did not relax the cardia in cases of achalasia (5).

Cardiospasm and Hirschsprung's disease (congenital megacolon) may be related etiologically. In both diseases, dilatation of organs and absence of intrinsic ganglion cells has been reported. Lately, our views on the role of degeneration of ganglion cells in the etiology of megacolon have changed. It was believed formerly that the part of the colon with degenerated intrinsic ganglion cells dilated for lack of cholinergic and prevalence of adrenergic innervation. However, it has been demonstrated recently by more extensive histologic studies, that a contracted portion of colon below the dilatation had lost its intrinsic ganglion cells, while the dilated part was normal in that respect. Henceforth, resection of the contracted part was undertaken, and the results in cases with true Hirschsprung's disease justified the assumption (6). Similar studies in cases of achalasia of the cardia are desirable.

It is possible that a reflex disturbance causing cardiospasm, such as may originate from gallbladder disease, appendicitis, etc., can lead to achalasia by the following sequence of events.

In the presence of reflex cardiospasm, stasis of food, fermentation, and infection, may occur and produce considerable irritation of the mucus membranes of the esophagus, with esophagitis, erosions, ulcers, etc. The irritation of the esophagus may set up local reflexes to the cardia, and a vicious circle may result from distant and local reflexes. In the course of time, inflammation may produce degeneration of intrinsic plexuses, aided by pre-existing or secondary vitamin deficiency.

There are short reflex arcs along the entire gastrointestinal tract, and sensory receptors probably are in the mucus membranes. The possible presence of axon reflexes in the gastro-intestinal tract has to be con-

sidered, which could produce spasm of smooth muscle and dilatation, stasis and exudation from capillaries and arterioles.

Local reflexes from an irritated lower esophagus which may produce or abet achalasia, may be interrupted by local application of surface anesthetic drugs. Distant reflexes which may produce cardiospasm, such as from peptic ulcer, diaphragmatic hernia, gallstones, etc., can be abolished by interrupting the reflex with spasmolytic drugs; in other words, if spasm in the duodenal bulb or the bile passages is abolished, reflex cardiospasm would disappear.

In previous experiments in animals and in man, we have demonstrated that a small dose of certain local anesthetic drugs applied locally to the intestinal mucosa, produced a greater local relaxation than the same or even larger doses injected intravenously (7-9).

On the basis of the above considerations and the results of our experiments, we have treated cases of cardiospasm by oral administration of topical anesthetic drugs. The drugs were dissolved either in syrup or in carboxymethylcellulose, to maintain contact with the surface and prolong the local effect. Also, the viscid solution prevented undue diffusion of the drug on the oral mucosa, thus avoiding numbness of tongue and buccal surfaces.

We have been encouraged in our present work by the appearance of a new drug which has both spasmolytic and topic anesthetic properties, and possesses such a degree of tolerance, that even large doses did not produce undesirable reactions. This drug is JB 305 (Dactil, Lakeside), N-ethyl-3-piperidyl-diphenylacetate hydrochloride (10). In tests in animals and man, it has been found to possess low toxicity and rapid onset of action, and it has been used safely in patients (11). In our own animal experiments, we have found JB 305 to have rapid spasmolytic effects, within a few minutes after subcutaneous or intravenous administration and within approximately 10 minutes following oral administration.

Two criteria were used for effectiveness of the drug in cases of cardiospasm. First, control X-ray films with barium suspension were taken, and the emptying time of the barium into the stomach was recorded. A day later, JB 305 in solution was administered, barium was given immediately thereafter, and X-ray films were taken 5 and 10 minutes later. The second criterion was based on subjective effectiveness, that is the patient's response.

Four cases of cardiospasm of whom 3 were treated with JB 305, are reported below:

Case No. 1: An undernourished 13-year-old white girl, weighing 50 pounds. The child entered Sarah Morris Hospital with a diagnosis of pneumonia. X-rays and sputum tests indicated lipid pneumonia. Consequent history revealed that the patient was constipated chronically and had received mineral oil every night.

*From the Department of Gastro-Intestinal Research, Medical Research Institute of Michael Reese Hospital, Chicago, Illinois.

Supported by a grant from the Lakeside Laboratories, Inc., Milwaukee, Wisconsin. The Department is in part supported by the Michael Reese Research Foundation.

An unexpected finding in X-ray films of the chest was a dilated esophagus and a contracted cardia. Apparently, the mineral oil which was administered at night, floated on top of the contents of the esophagus, entered the throat during sleep, was aspirated into the lungs, and had caused lipid pneumonia. X-ray studies showed that the contents of the esophagus emptied into the stomach over many hours. At that time the author was interested in Trasentin (diphenylacetyl-diethyl-aminoethanol HCl), a drug which has both spasmolytic and topic anesthetic properties (12, 13). Half an hour before meals the contents of the esophagus were aspirated and one tablespoonful of raspberry syrup, containing 50 mg of Trasentin, was given by mouth. Following the first treatment, cardiospasm disappeared and the barium meal entered the stomach rapidly. The girl was able to eat normally and gained weight. When the drug was discontinued, cardiospasm recurred.

Case No. 2: A 10½ months white male infant, weighing 17 pounds, was admitted to Sarah Morris Hospital. X-rays showed considerable dilatation of the esophagus and cardiospasm. The child regurgitated and, although some food passed into the stomach slowly, a serious nutritional difficulty existed. The child was treated with syrup containing 10 mg of JB 305 per teaspoon. X-ray films demonstrated rapid emptying of barium into the stomach within less than 10 minutes after administration of the drug. Subsequently the infant received 10 mg of JB 305 before every meal. It made satisfactory progress and gained in weight. Figures 1 and 2 demonstrate the effects of the drug.

Case No. 3: V. W., 26-year-old white female entered Michael Reese Hospital* with complaints of difficulty



Fig. 1. Case No. 2: Infant, male, 10.5 months. Cardiospasm. Thirty minutes after administration, no barium in stomach.

*We are obliged to Dr. M. J. Colletti for this case.

in swallowing and loss of weight. X-ray films demonstrated distinct dilatation of the esophagus and cardiospasm. Emptying of barium meal from the esophagus took 30 to 60 minutes. JB 305, 200 mgs in syrup, was administered 30 minutes before meals. The patient reported immediate beneficial effects. Substernal discomfort, which before occurred with every meal, disappeared and she was able to eat regularly and enjoy her food. X-ray films demonstrated that JB 305 did not speed up emptying of the barium meal into the stomach, although esophageal peristalsis seemed to increase. In this case we assume that the effect of JB 305 was diminishing the pain caused by overdistention and by the peristaltic movements of the esophagus against the mass of food.

Case No. 4: L. C., a 60-year-old colored female. The patient's complaints were difficulty in swallowing and choking, sticking of food in her throat while liquids passed easier, weight loss of 41 pounds during the last 4 years, and paroxysmal nocturnal dyspnea; pain in mid-epigastrium and knife-like pain to the back from below the sternum, relieved by sodium bicarbonate. Esophagoscopy and X-ray studies showed a dilated esophagus and narrowed cardia, ineffective esophageal peristalsis, and an ulcer crater in the duodenal bulb.

The effects of JB 305, 200 mgs in syrup, administered before meals were similar to those in patient No. 3. The discomfort associated with eating of solid foods disappeared, there was no choking, no substernal pain, and she was able to eat normally. In 2 weeks on this therapy, she gained 4 pounds. However, X-ray films failed to confirm the physical improvement. Barium stayed in the esophagus about as long as previous to therapy with JB 305. Therefore, we assumed that, like in patient No. 3, the effect of the drug was upon pain receptors in the esophagus and that her improvement was due to the loss of discomfort and pain.



Fig. 2. Case No. 2: Same patient. JB 305, 10 mg in syrup before barium. Film taken approximately 8 minutes after JB 305. A relatively large amount of barium has entered the stomach. Note peristalsis, pushing barium up into esophagus and down into stomach.

DISCUSSION

We are reporting results on 4 successive cases, because medical therapy in cardiospasm so far has been discouraging. The clinical results in our cases are such, that we feel justified in reporting them, so that JB 305 can be evaluated clinically on a larger scale. In cases of cardiospasm, topic anesthetic-spasmolytic drugs seem to take effect by various mechanisms. They abolish local pain, they abolish local reflexes, and they act as anticholinergic spasmolytic agents.

It is possible that local anesthetic-spasmolytic drugs can be employed in the treatment of other conditions, such as functional bowel obstruction (8, 9); their use in the treatment of gastric ulcer and pylorospasm has been reported but has not been accepted widely (9).

Recently, we have observed 4 cases of cardiospasm in which cancer of the upper part of the stomach was found later. Apparently, carcinoma of the stomach can produce cardiospasm by irritation and reflex, in the absence of infiltration of the cardia. In these cases, X-rays did not demonstrate the malignancy until long after cardiospasm had been noted. This experience should warn us to think of possible cancer of the stomach in cases of cardiospasm and not to delay repeated clinical and laboratory examinations. In such cases, success of medical treatment of cardiospasm would lull both, patient and physician, into a sense of false security.

Ingelfinger and coll. (2, 3) have reported that mecholyl produced motility of the esophagus in cases of achalasia of the cardia, while in normal subjects it did not show much effect. We have found earlier, that prostigmine exerted a muscular effect on the esophagus in completely atropinized dogs. This may mean that cholinergic drugs affect the esophageal musculature also by direct musculotropic effects and that even in the absence of cholinergic innervation, certain cholinergic drugs can be effective (14).

SUMMARY

The medical treatment of selected cases of cardiospasm is discussed. A new drug, JB 305, has been used successfully. JB 305 is fast acting, has low toxicity, and no undesirable effects of any kind were noted.

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COMPLETE NON-ROTATION OF THE GUT AND TORSION OBSTRUCTION OF THE COLON IN AN ADULT (Case Report)

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THE EMBRYOLOGICAL development of the gut is productive of many anomalies and irregularities. Among the most frequent developmental anomalies are

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those produced by some degree of failure of the rotational process. Errors in rotation of the gut are frequently associated with excessively long mesenteries of various parts of the bowel. Rarely, rotation of the gut may fail to occur; in this event the various bowel segments occupy a fetal position. This fetal configuration is extremely rare and seldom reported in the adult; while partial rotational anomalies are relatively common, being most frequently seen as misplaced cecums.

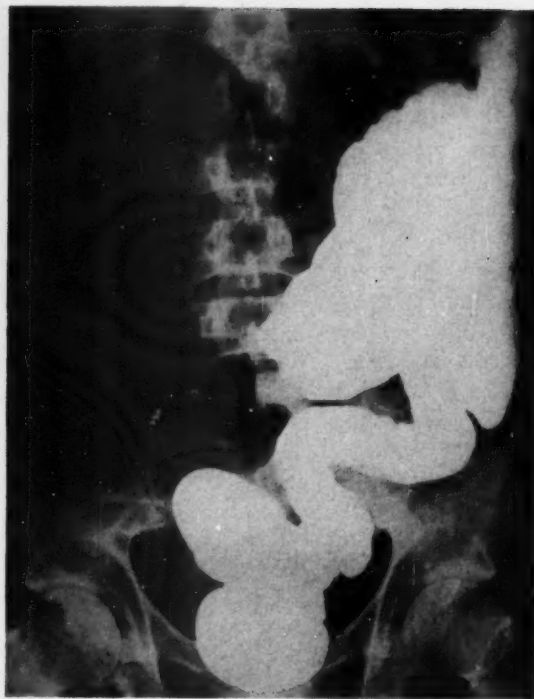


Fig. 1, A and B: Illustrating the typical roentgenographic characteristics of ceco-colonic torsion, as suggested by the large cecal gas bubble demonstrated on the scout film and confirmed by barium enema.

The case described herein is unique in that it represents a completely non-rotated bowel in an adult producing classical physical and roentgenologic findings of torsion of the cecum.

CASE REPORT

I. C. B.—A 31-year-old white male was admitted to the hospital in acute delirium tremens and suffering with a bowel obstruction (10-26-51). There was a history of having had an operation elsewhere one year prior to this admission, at which time the appendix was removed and "some twisted bowel was corrected." The delirium was treated, and the bowel was decompressed by nasogastric suction. The obstruction was found to be incomplete, and it was believed to be due to adhesions secondary to the previous laparotomy. This was supported by the fact that a ventral hernia was demonstrated in the scar. The bowel was prepared with aureomycin and after restoration of the electrolyte balance, a laparotomy was done (11-5-51). A loop of proximal ileum was found adherent to the old laparotomy scar and was believed to be the cause of the obstruction. This segment of ileum was resected and an end-to-end anastomosis was done. Because of the acuteness of the disease an abdominal exploration was omitted. An uneventful recovery followed this operation.

On February 26, 1952, he was operated upon again, at which time additional adhesions were divided, a biopsy of mesenteric lymph node was obtained and a ventral, incisional hernia was repaired. At this op-



Fig. 2: Postoperative appearance of the colon after fixation by cecostomy, indicating a more normal location. Compare with Fig. 4.

eration it was noted that a rotational anomaly of the colon was present. Recovery from this procedure was uneventful, and he was discharged on March 8, 1952. He remained well and was seen at intervals until October 15, 1952, when he was again hospitalized because of tarry stools and hematemesis, which began three days prior to admission. Two weeks later, while still in the hospital for study, he suddenly developed abdominal cramping and progressive distention with tenderness in the right lower quadrant. A diagnosis of large bowel obstruction due to postoperative adhesions was made. A scout film of the abdomen revealed a gas-filled cecum, but no gas distal to the hepatic flexure. A barium enema disclosed an obstruction in the midportion of the transverse colon. The radiographic impression was "volvulus of the cecum and ascending colon possibly associated with an adhesion band."

On October 30, 1952, the abdomen was explored through a transverse incision, and complete non-rotation of the bowel was demonstrated. The cecum and ascending colon, which were on a long mesentery, had rotated on the mid-colon in such a manner as to produce a torsion of the mid-colon resulting in bowel obstruction. The torsion was reduced by rotating the cecum in a counter-clockwise manner. Fortunately no

vascular damage had occurred, and the bowel was viable. Because of the massive dilatation of the cecum it was believed to be unwise to suture the thinned and edematous wall. However, fixation of the cecum was obviously necessary to prevent recurrence of the condition. A cecostomy was therefore performed in the right lower quadrant in order to decompress the bowel and simultaneously to provide a firm point of fixation of the cecum to prevent further torsion. Recovery from the operation was uneventful; the cecostomy was closed on November 12, 1952. On November 25, 1952, a thrombosed external hemorrhoid was excised, and the patient was finally discharged on November 26, ambulant and with no complaints.

DISCUSSION

Excess mobility of the cecum is always associated with an abnormally long mesentery of the proximal colon which may result in a mechanical bowel obstruction, described as volvulus or torsion. Neither of these terms, in their commonly accepted usage, is perfectly descriptive of the pathologic process. Torsion usually implies a twisting on a pedicle, and volvulus a twisting of the bowel on its mesentery. In both instances the pathologic process involves obstruction of the blood supply with resulting gangrene of the or-

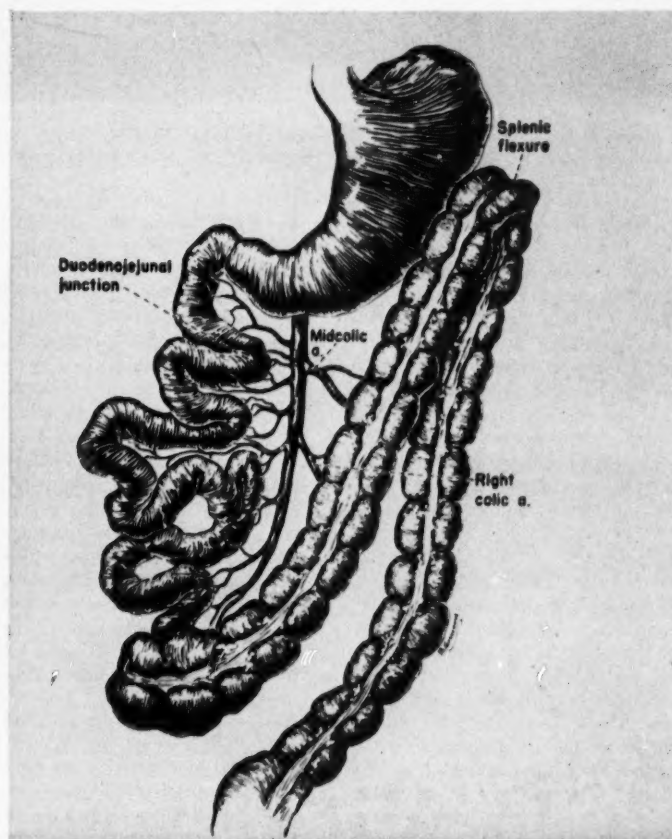


Fig. 3: A diagrammatic representation of the arrangement of the bowel in this patient, indicating a typical fetal disposition of the gut. Note in particular its relation to the superior mesenteric artery.



Fig. 4, A and B: Preoperative pre- and post-evacuation roentgenograms of a barium enema demonstrating the fetal position of the colon and its location in the left side of the abdomen. Compare these roentgenograms with the diagram in Fig. 3.

gan involved. An excessively mobile cecum, on the other hand, will produce bowel obstruction without gangrene because it is a torsion of the cecum on the colon, and the long mesentery wraps itself about the cecum without interfering with the blood supply. This accounts for the fact that gangrene is so rarely described as a result of cecal torsion. It is possible that the term "ceco-colonic torsion" might be more descriptive of the condition. If a vascular component of ceco-colonic torsion obtains, it is more likely attributable to the extreme cecal distention proximal to the point of obstruction than to vascular occlusion. Untwisting the bowel results in a rapid remission of symptoms.

The diagnosis of ceco-colonic torsion is relatively simple (2, 7). The gas bubble representing the dilated cecum in the right lower quadrant is identifiable by palpation and percussion on physical examination, as well as by roentgen examination (Fig. 1). A barium enema confirms the diagnosis and may indeed reduce the torsion. These facts are well established, and this case is reviewed to emphasize that such conditions may occur in adults, as well as to present the typical picture. The history is of little help in diagnosis except that adults may have a long history of intermittent, vague abdominal symptoms. The treatment is a restoration of the normal relations of the cecum and colon with fixation of the cecum to the abdominal wall (Fig. 2). If fixation is omitted,

a recurrence of the condition can be expected. The cecum may be fixed by suture if the bowel wall is healthy. However, if massive distention and thinning of the cecal wall has occurred, appendicostomy or cecostomy are simple and safe procedures which accomplish not only fixation of the bowel but also permit decompression.

The really unusual feature of the case is the fetal position of the gut in an adult (5). As demonstrated in Figure 3, the bowel in this patient lay in the fetal position so that the duodenal-jejunal junction was to the right of the superior mesenteric artery. A long mesentery was present which ran for the entire length of the gut, the only point of fixation being at the splenic flexure. This resulted in the small bowel being mostly confined to the right side of the abdomen with the colon occupying the left side (Fig. 4).

In the case reported it is quite probable that the entire chain of events was due to recurring ceco-colonic torsion. The significance of the patient's statement that "some twisted bowel was corrected" at his first operation was not appreciated at first. Indeed, it is quite likely that the bowel obstruction which next occurred and which was believed to have been caused by the adhesion of the ileum to the laparotomy scar might well have been a recurrent torsion. At his third laparotomy, for repair of the incisional hernia, the incomplete rotation of the bowel was discovered, and at this time the cecum should have been fixed. Had this been done, he would have been saved a final operation.



Fig. 5: A diagram illustrating the mechanism of ceco-colonic torsion.

SUMMARY

A case of non-rotation of the bowel complicated by large bowel obstruction distal to the cecum has been described. The obstruction was produced by the rotation of the cecum in a clockwise fashion on its long axis. This obstructive process has been variously described as cecal torsion or volvulus. We submit "ceco-colonic torsion" as a much more precisely descriptive term. Cecal fixation is essential in treatment to prevent recurrent obstruction.

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GASTROSCOPIC EXPERIENCES IN THE UNITED STATES ARMY, EUROPE

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THE PRESENT report covers a period of three years, from March, 1950 through March, 1953, during which gastroscopic examinations were conducted on the medical service of the 98th General Hospital, Munich, Germany, and includes all but a few of such procedures in the Command during this time. Cases received for consultation, in addition to those routinely referred from the medical and surgical services of this General Hospital, were sent from other Army and Air Force installations, and a few were performed at the request of the medical staff of the University of Munich.

TOTAL PROCEDURES AND SELECTION OF PATIENTS

A total of 1186 gastroscopies were performed in 925 patients, 864 of whom were males, and 61 females. There were 41 failures not included in these figures, the reasons for which will be discussed subsequently. The relatively large number of female patients in a predominantly male group is explained by the fact that in this command service installations care for the majority of dependents of service personnel, as well as for government employees in the theater. Indications for gastroscopy on our service are relatively wide in latitude, and it is considered routine in any cases where it might possibly give information and where there are no contraindications. Figure No. 1 demonstrates relative proportions of gastroscopic findings.

MATERIALS AND METHODS

The Eder-Chamberlin gastroscope with controllable tip was used in all cases (8). This instrument has proved superior in our experience because of improved definition of the area seen, better lighting, and increased ability to visualize the antrum and posterior wall of the stomach. No difficulty was encountered in using either the bullet- or finger-type tip. It is felt that perhaps the former is more maneuverable within the stomach when the tip is manipulated. Due to the increased length of the rigid portion, this instrument must be introduced gradually, but with gentle pressure and cooperation on the part of the patient, passage is no more difficult than with the standard type of flexible gastroscope. Pre-operative medication included .1 gm. of Seconal one hour before examination, 50 mg. of Demerol and 1/150 gr. of Atropine one-half hour previous. The stomach was not evacuated by tube, and a darkened room was not found to be necessary prior to passage of the instrument and visualization. Every effort was made to present the procedure as a routine diagnostic measure, and patients reacted well to this orientation.

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NORMAL STOMACHS

Negative findings, or minor changes not thought to be significant were noted in 694 instances on 650 patients, or 70.3 per cent of the total number examined. These figures reflect: 1) the concept of gastroscopy as a rather routine procedure, 2) rigid criteria in the evaluation of minor changes in the gastric mucosa, especially in gastritis, 3) the time interval in referral of many cases for consultation, and 4) the predominantly young, service type of personnel examined. The finding of a normal stomach serves a useful purpose for both the patient and the operator in evaluation of symptoms, hence it is felt that many normal stomachs will be viewed if enough gastroscopies are done. Overinterpretation, especially in possible gastritis changes, has been warned against by other observers (14, 17), and we have felt that this attitude is essential to proper evaluation. The time interval is an important one in service installations, since several weeks may pass before referral to the consultant, and during this period many ulcers as well as minor mucosal lesions may heal. In this connection, 39 cases of the normal group were referred because

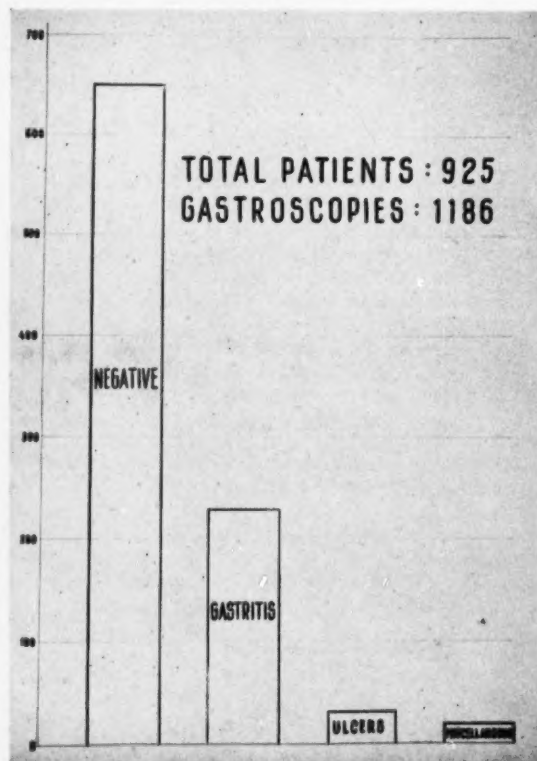


Figure 1

of x-ray findings suggestive of gastric ulcer, which could not be confirmed either by x-ray or gastroscopy in our hospital. Several of these had rather definite findings on transfer films, and it could only be inferred that the ulcer had healed between examinations (26). Most of the presumptive ulcers were referred with suspicious antral deformities which were shown to be spasm by complete visualization of the antrum plus negative x-ray evaluation. It was deemed necessary to view the entire antrum, however, before declaring it negative. Duodenal ulcer was proven by x-ray in 97 instances in this group of normals. It has been routine to gastroscopically examine all patients with duodenal ulcer on our service, and total results will be discussed later.

FAILURES

Gastroscopic failures were encountered in 41 patients. Of these, the instrument could not be passed in 17, 20 were so uncooperative as to necessitate discontinuance of the procedure, and incomplete visualization was obtained in 4. Several patients required 1-3 attempts before a satisfactory examination could be obtained, and are not included in the group, but serve to emphasize that where no contraindications exist repeated efforts may be rewarding.

COMPLICATIONS

Two accidents occurred during this period. In one instance, pneumo-peritoneum with mediastinal and subcutaneous emphysema developed following uncomplicated passage, and was treated conservatively with complete and early recovery. This case has been reported (18). The second patient suffered a perforation high up in the esophagus when he suddenly became extremely active during the attempt to pass the instrument, although he had previously shown no sign of becoming uncooperative. He was explored, but because of its high location the perforation could not be closed. Recovery was complete but prolonged following the development of a fistula, and he is now on full duty.

DIVERTICULA

Three gastric diverticula were referred following x-ray diagnosis. This finding is relatively rare (4). The ostia and a portion of the floor were visualized in all three, which were conventionally located in the

cardiac portion of the stomach. Two, which opened more toward the lesser curvature side, occurred in patients who exhibited primarily functional complaints, in whom no other diagnosis could be made, and who were discharged to duty. The ostium in one of these appeared to show a type of peristaltic activity, while in the other the closing and opening was synchronous with breathing and appeared to depend on stretching and relaxation of the stomach wall during respiration. A photograph of one of these is shown in Figure 2.

The third patient, an Army nurse aged 34, was seen to have an opening directly on the posterior wall of the stomach. The ostium remained fully open, and a portion of normal-appearing mucosa could be visualized on the floor of the diverticulum. She had had definite recurring attacks of nausea, vomiting, and epigastric pain, with otherwise negative findings throughout the gastro-intestinal and biliary tract. Operation showed the distal portion of the diverticulum to be bound down to underlying structures, with considerable inflammation of the peritoneal mucosa. Resection provided complete relief of symptoms. The gastric mucosa in all three patients was normal gastroscopically.

POST-OPERATIVE STOMACHS

Examination of post-operative stomachs was carried out in 12 patients, in whom 26 gastroscopies were performed. All had had resections with varying amounts of the stomach removed. Findings of gastritis in all but two agree with observations of others (6). Functioning gastro-enterostomy openings were visualized in all 12. Stomal erosions were noted in 2, and a small stomal ulcer in 1, all of which were observed to heal under ulcer therapy. An ulcer involving the area 1 cm. above the gastro-enterostomy opening was observed in a male soldier with ulcer-like symptoms, in whom only the antral area of the stomach had been removed for a perforated gastric ulcer. On exploration he was found to have an ulcerated area secondary to a large cotton suture buried in this location. A civilian female patient of this group who had had a resection for carcinoma of the stomach with metastasis showed a large hemorrhagic area just above her gastro-enterostomy opening. She was explored, but the area could not be identified at operation, and no evidence of further carcinomatous involvement could be found.

The x-ray examinations on this entire group showed functioning gastro-enterostomy openings without demonstrable pathology of the remaining stomach. It is felt that gastroscopic follow-up in all post-operative stomachs is essential to proper evaluation of such cases, and should be performed whenever symptoms would indicate or when routine x-ray examinations are done post-operatively (13, 6).

GASTRIC TUMORS

Three instances of tumor formation without ulceration were seen. One of these, shown by x-ray as an annular constricting lesion of the antrum, showed a fixed angulus and immobile antrum on two examinations. Operation revealed an annular carcinoma of the antrum without mucosal ulceration. A second patient was found to have a tumor of the lesser cur-



Fig. 2: Ostium of diverticulum with barium evacuating.

vature side of the antrum, and a third a fungating lesion of the greater curvature. Atrophic gastritis of moderate to severe degree was observed in all three cases. X-ray had failed to show the greater curvature lesion on four occasions, but was positive in the other two cases.

GASTRIC ULCERS

Ulcerations were noted in 30 patients. Of these, 2 were visualized by x-ray and not by gastroscopy; 10 by gastroscopy but not by x-ray, and 18 were found both by x-ray and gastroscopy. In only 1 of these was the diagnosis of carcinoma made pre-operatively by gastroscopy, whereas actually 3 were found to be malignant on operation. The two ulcers not definitely diagnosed as carcinoma, however, were found only by gastroscopy and operation advised when they failed to heal within four weeks' time. Observation to complete healing was carried out in 21 under gastroscopic control, and 6 others were resected and found to be benign when healing was felt to be delayed.

The relatively large number of ulcers seen gastroscopically and not by x-ray examination is felt to be partly due to the time interval in referrals previously mentioned, since several were obviously well along in healing when seen, and craters could not be found by x-ray. Conversely, however, it is felt that all gastric ulcerations should be followed by gastroscopy to complete healing, and that degrees of progress in healing may be noted more readily in this manner (13).

ADENOMATOUS POLYPOSIS

In 2 cases, single small sessile polyps of the antral region were noted, and 1 instance of diffuse adenomatous polyposis was viewed by the gastroscopist following x-ray diagnosis. This was a 43 year old civilian female who complained only of occasional vomiting, which was followed by rather intense headaches. The attacks had been occurring sporadically for 2½ years, but had increased in frequency over the past few months. At gastroscopy approximately 30 polyps of all sizes, mostly sessile, but a few pedunculated were

visualized, two of which were large, dark and hemorrhagic-looking. The antrum showed some roughening of the floor, part of the angulus appeared fixed and there was encroachment by a polypoid mass. Photographs of several areas were taken and are shown in Figure 3. The cardiac portion of the stomach showed only 5-6 small, well-pedunculated polyps. Pictures and description served to orient the surgeon prior to operation, at which the gastroscopic impression was confirmed, and a subtotal resection performed. Adenomatous polyposis of this type is infrequently seen, although several excellent reviews of the subject have been made (5, 25).

GASTRITIS

The clinical diagnosis of gastritis is one frequently seen in patients referred to service installations for gastro-intestinal consultation. Substantiation can only be made by gastroscopy (24, 12, 10), and it has been our experience, as well as that of others (15, 17) that no definite symptom complex is associated with the various types. Consequently, although the diagnosis was made in 227 patients, or 24.5 per cent of those examined, there were few cases where the clinical impression coincided with the gastroscopic findings. Nevertheless, there is little doubt that some types of gastritis do give symptoms which may be at times disabling, and these types are prone to occur in service personnel, as well as in the general population (14, 17, 11).

Schindler's classification has been used in all cases in our series, and the five general types encountered are listed in Table 1. In an attempt to assess the numbers of each type with and without association with duodenal ulcer, the figures have been broken down into numbers and percentages in these groups. It will be noted that while there is only slight divergence of total figures, hypertrophic gastritis occurred twice as frequently in duodenal ulcer patients, and no cases of atrophic gastritis were seen in the duodenal ulcer group. The low total figures for this group are in agreement with Schindler (24) and Church (9), but in disagreement with some observers (7). Those classi-

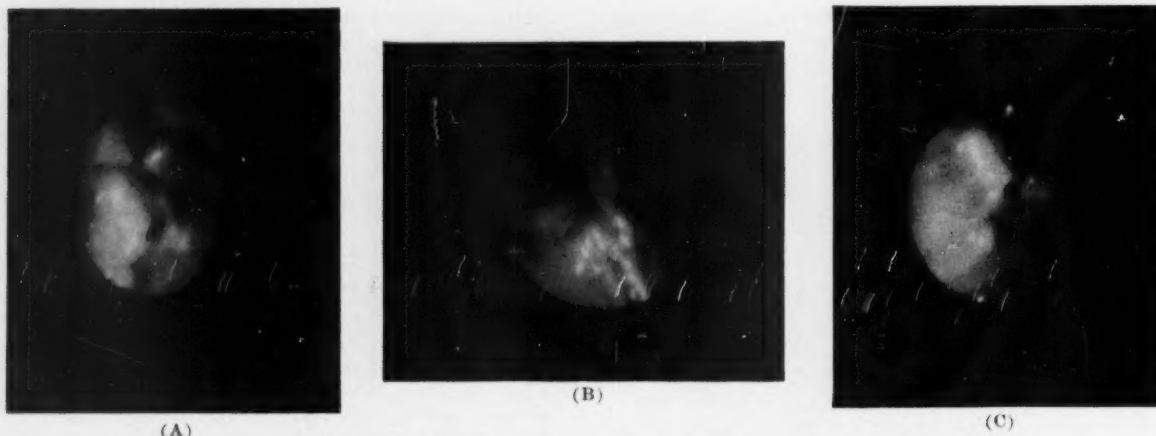


Figure 3: Adenomatous Polyposis

- (A) Shows large hemorrhagic polyp of lesser curvature.
 (B) Polypoid masses at angulus, base of which is seen at right.
 (C) Sessile polyps of greater curvature.

TABLE I
GASTRITIS FINDINGS

Type	Gastritis		Associated with Duodenal Ulcer (134 Cases)		Not Associated with Duodenal Ulcer (791 Cases)		Associated with Hemorrhage Only
	No.	%	No.	%	No.	%	No.
1. Superficial	108	47.5	14	10.4	94	11.9	14
2. Hypertrophic	59	26.0	15	11.2	44	5.6	2
3. Atrophic	26	11.5			26	3.3	
4. Hypertrophic & Superficial	26	11.5	6	4.5	20	2.5	
5. Atrophic & Superficial	8	3.5	2	1.5	6	.8	
Totals	227	100.0	37	27.6	190	24.1	16

fied as "hemorrhage only" are cases in which the gastritis was the only demonstrable source of bleeding. That hemorrhage even in gross quantities may be the result of gastritis has been well documented (1, 21). A total of 371 gastroscopies was performed, which reflects follow-up studies in most cases, especially those of the superficial type.

Superficial gastritis, as noted in Table 1, was most frequently seen. The criteria for this diagnosis were patchy reddening, usually around areas of erosion covered by thick adherent mucous, involving any or all areas of the stomach. Care was taken to include no instances of mere "red stomach." The 14 cases of hemorrhage in this group were all found to have deep erosions, mostly multiple. Two involved only the tops of rugae, but the others the inter-rugal mucosa. Symptoms in superficial gastritis were not severe, but all cases were followed gastroscopically to complete or almost complete healing. Hemorrhagic erosions in particular necessitated gastroscopic clearance before

discharge. All cases in this group were returned to duty, or in the cases of civilians, discharged to home.

Hypertrophic gastritis was diagnosed only when, in addition to the usual swelling of the mucosa, there were definite granular "cobblestoned" areas between the rugae, although these might also involve the rugae. This type of gastritis was in our experience the most productive of chronic symptoms and disability, especially among the service group. There were 5 cases in this category showing definite polypoid changes. These were noted to involve the greater curvature primarily in 4 cases, while in another the heavy polypoid masses almost filled the entire stomach cavity. The post-operative specimen of this 30 year old sergeant, in whom a total gastrectomy was done, is shown in Figure 4. It is interesting to note that even with this amount of involvement, the correct diagnosis could only be made by gastroscopy, which was exceedingly difficult due to the non-distensibility of the stomach and the small amount of space available for the gastroscope. Another patient, a 29 year old enlisted man, had been followed for five months on duty by gastroscopy after prolonged treatment. He returned with ulcer-like symptoms, was found to have a gastric ulcer which did not heal under therapy, and underwent subtotal resection. The post-operative specimen is shown in Figure 5. Two other cases are still being followed on duty, and another with severe polypoid involvement refused operation and was transferred to the United States. Although we agree with others that minor hypertrophic changes may regress (15), it would appear that when severe polypoid changes are found nothing avails and the patient will eventually be disabled. There is also the problem of distinguishing these areas from malignant infiltrations, and the question of whether they may not be precancerous foci (22, 24, 25).

Atrophic gastritis was seen relatively infrequently, and all but a few cases had a patchy, rather than generalized, involvement. The criteria of greyish mucosa, thin enough to show the underlying vessels, is well known, and was adhered to strictly in diagnosis. Sym-

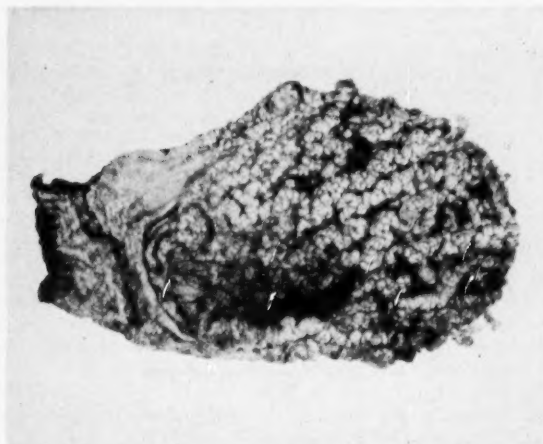


Fig. 4: Hypertrophic polypoid gastritis which almost occluded the stomach cavity, total gastrectomy.



Fig. 5: Hypertrophic polypoid gastritis with ulceration. Ulcerated area may be seen in the narrowed mid-portion of the specimen. Subtotal gastrectomy.

toms were severe only in the generalized cases, one of which was sent to the Zone of the Interior, and another of which is still under observation.

Hypertrophic and superficial and atrophic and superficial types appeared to resemble the hypertrophic and atrophic clinically, and showed no special features.

DISCUSSION

The value of gastroscopy has been amply documented, and its employment as a routine method of diagnosis is felt to be justified in any case of gastro-intestinal symptoms where there are no contraindications and information might conceivably be obtained (13, 19). Its risk is low, and while it largely complements roentgenologic findings, there are types of gastric pathology more readily delineated and evaluated by its use. As gastroscopy is employed more routinely, the relative numbers of normal stomachs viewed will increase, but it is felt that this trend is a healthy one, since a normal gastroscopic examination gives information obtainable in no other manner.

SUMMARY AND CONCLUSIONS

1. Over a 3 year period, 1186 gastroscopies were performed in 925 patients in an Army General Hospital of the United States Army, Europe. Of the total, 650, or 70.3 per cent, revealed normal findings. This number is somewhat greater than those of other series, but is probably due to more routine use of gastroscopy in cases of obscure gastro-intestinal symptoms, plus the type of patient seen, time interval in referral, and conservatism in interpretation. Negative findings serve a definite purpose.

2. Two complications, one a case of pneumoperitoneum and the other a perforation of the upper esophagus in an uncooperative patient, are reported.

3. Miscellaneous findings of interest included: 1) 3 diverticula, one of which was removed surgically; 2) 3 gastric tumors without ulceration, and 3) 1 case of adenomatous polyposis.

4. Gastric ulcers were relatively few (30 cases). Gastroscopy is believed superior to x-ray in the follow-up of these lesions, and in the diagnosis when the referral interval has been several weeks, as in many of our series.

5. Gastritis provided the majority of the gastroscopic findings, and the relative incidence in duodenal ulcer and with associated hemorrhage for which no other cause could be found, are shown. Hypertrophic gastritis was found to produce the most severe clinical symptoms, and 5 with moderate to severe polypoid formation were observed, two of which underwent resection. Superficial gastritis was the most commonly noted form (47.5 per cent), but had fewest associated symptoms and the least chronic course, although it was the most frequent producer of hemorrhage (14 cases). Atrophic and mixed types were relatively infrequent.

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STUDIES OF AEROGENIC AND ANAEROGENIC VARIANTS OF SALMONELLA SCHOTTMUELLERI II. RESISTANCE TO ANTIBIOTICS AND SULFADIAZINE

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THE LITERATURE dealing with bacterial resistance to chemotherapeutic agents is voluminous. The number and diversity of reports on this subject indicate a need for additional evidence which might correlate such resistance not only with recognizable attributes of particular species of bacteria, but also with their culture states such as mucoid, smooth, and rough.

The significance of colonial phases in infections has been reviewed by Hadley (1937). In this paper and in a subsequent report, Hadley (1939) points out that among the various families of bacteria, certain major colonial phases (mucoid, smooth, or rough) may be observed more often in one family than in others; also that these culture phases may be associated with relative degrees of resistance, virulence, etc. That more than one state of an organism can exist *in vivo* has been reported for members of the genera *Streptococcus* (Tunnick and Woosley, 1935; Hadley and Wetzel, 1946), *Mycobacteria* (Smithburn, 1935), *Neisseria* (Raven, 1934), *Salmonella* (Fletcher, 1918; Jungherr and Wilcox, 1934), and many others. Moreover, differences in resistance to chemical agents have been noted with differing colonial forms of *Pseudomonas aeruginosa* (Gainor and Williamson, 1951), *Brucella abortus* (Braun *et al.*, 1951), hemolytic streptococci (Hadley and Hadley, 1941), and pleuropneumonia-like bacteria (Dienes, 1947).

The purpose of this paper is to report experimental observations on the relative degrees of resistance manifested by stable* aerogenic and anaerogenic forms of a strain of *Salmonella schottmuelleri* (A.T.C.C. 9282) to various antibiotics and sulfadiazine.

MATERIALS AND METHODS

The following drugs were used in this study: aureomycin hydrochloride (Lederle Laboratories, Inc.); chloromycetin (Parke, Davis and Company); penicillin (crystalline) G potassium (Squibb and Company); streptomycin (crystalline dihydrostreptomycin) (Merck and Company); terramycin hydrochloride (Chas. Pfizer and Company); and sulfadiazine sodium (Squibb and Company).

Difco nutrient broth and nutrient agar were used throughout the studies. All cultures were subtransferred daily on nutrient agar for one week prior to use in the resistance tests. Bacterial suspensions were made from agar-slant growths 18 to 20 hours old. The purity of the colonial states was established by streak plates. More detailed information concerning the sta-

bility, origin, and biochemical characterization of the aerogenic and anaerogenic forms is reported in a previous paper (Weigle and Gainor, 1954). The designations for the various colonial forms are as follows: M₁, S₁, R₁ (aerogenic mucoid, smooth, and rough, respectively); M₂, S₂, R₂ (anaerogenic, mucoid, smooth, and rough, respectively).

Paper-disc tests.—Ten to twelve ml of nutrient agar were poured into petri dishes (95 mm), allowed to harden, and then incubated for 24 hours at 37 C. This incubation period afforded an opportunity to check sterility and to remove moisture at the surface. The sterile agar plates were then evenly overlaid with 6 to 7 ml of nutrient agar which had previously been inoculated with a suspension of the specific colonial form under investigation. The initial concentration of organisms per ml in the superimposed layer of agar was approximately 35×10^4 . Seven petri dishes of each of the colonial variants were plated in this manner. All tests were conducted in duplicate.*

Fresh concentrations of the antibiotics and of sulfadiazine were prepared in sterile distilled water (pH 7). Three filter paper discs (Schleicher and Schnell; analytical filter papers, 12.7 mm diameter) were used for each plate; each disc was inoculated with 0.08 ml of the desired concentration of the drug. Although aureomycin was not entirely soluble at a concentration of 20 mg per ml, agitation prior to inoculation permitted a uniform distribution of the aureomycin with no clumping on the surface of the discs.

The inoculated test plates were incubated in an upright position. After 24 hours at 37 C., zones of inhibition showing complete clearing were measured from the edge of the disc to the outermost point of clearing and the area recorded in millimeters.

Tube-dilution - subtransfer tests.—Freshly prepared concentrations of the respective drugs were made in sterile nutrient broth (pH 7). The final volume of these "original" tubes was 10 ml. A 0.1-ml suspension of the individual colonial forms was inoculated into these tubes, giving a final concentration of 35×10^4 organisms per ml of test solution. After periods of 10, 24, and 48 hours' incubation at 37 C., a subtransfer of one large loopful was made into 5 ml of nutrient broth. Tube readings were made 48 hours after inoculation. All tests were done in triplicate.

RESULTS

The data in Table 1 indicate that with the paper-disc method (a) the three most resistant colonial forms were S₁, S₂, and R₁; (b) the three most susceptible

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*Morphological and biochemical characteristics remained unaltered after nine months of continuous 48-hour subtransfers.

*The duplicate tests, employing different strains from representative colonial types were twice repeated at intervals of several months. These results agreed basically with the recorded data in table 1, although there were slight differences in the millimeter measurements.

TABLE I
RESISTANCE OF AEROGENIC AND ANAEROGENIC COLONIAL VARIANTS OF
SALMONELLA SCHOTTMUELLERI TO ANTIBIOTICS AND SULFADIAZINE
AS MEASURED BY THE PAPER-DISC METHOD

Colony Type	Aureomycin			Chloromycetin			Penicillin			Streptomycin			Terramycin			Sulfadiazine	
	1600	160	16	80	16	1.6	52.8*	26.4	5.28	1600	160	16	80	16	1.6	1600	160
Zones of inhibition** in millimeters after 24 hours at 37° C.																	
M ₁ †	15	7	1	13	12	4	13	9	1	9	4	0	7	5	1	12	3
S ₁	7	2	0	9	7	0	9	8	0	7	2	0	5	0	0	0	0
R ₁	7	2	0	7	5	0	9	7	0	6	0	0	6	0	0	0	0
M ₂	17	10	3	14	12	5	15	13	2	13	11	3	7	5	1	15	5
S ₂	8	4	0	8	7	0	9	8	0	5	2	0	5	0	0	0	0
R ₂	12	8	2	15	12	7	13	9	3	10	5	0	11	9	2	17	5

*After the completion of this study we learned that 1509 units of penicillin were equal to 1 mg of penicillin (dry weight). Our use of 1000, 500 and 100 units consequently accounts for the odd concentrations.

**No increase in size of zones after 48 hours incubation.

†M₁, S₁, and R₁ = aerogenic mucoid, smooth and rough colony types respectively; M₂, S₂, and R₂ = anaerogenic mucoid, smooth and rough colony types respectively. Approximately 35x10⁴ organisms per ml of agar were plated.

forms were M₁, M₂, and R₂; (c) the two most effective antibiotics were penicillin and chloromycetin; (d) terramycin, aureomycin, and streptomycin followed in that order; (e) sulfadiazine was of the same order of effectiveness as aureomycin against the three most susceptible forms, but least active of all the drugs against S₁, S₂, and R₁. It is interesting to note the comparable efficiencies over relatively wide ranges of concentration of chloromycetin (80 µg to 16 µg per disc) and penicillin (66 µg to 33 µg per disc).

With the tube-dilution - subtransfer method, the results in Table 2 indicate that (a) the greater resistance of S₁, S₂, and R₁ was substantiated; (b) the greater susceptibility of M₁, M₂, and R₂ was likewise verified; (c) whereas penicillin was the most effective drug, chloromycetin was least efficient of the antibiotics; (d) terramycin and aureomycin were equally effective, followed by streptomycin; (e) sulfadiazine was practically ineffective against all colonial forms except R₂. All drugs manifested bacteriostatic and/or bactericidal capabilities if permitted to act for 48 hours.

DISCUSSION

The results reported in this study have afforded a number of opportunities for evaluating *in vitro* relationships between different colonial forms of *S. schottmuelleri* and their relative sensitivity to drugs. The validity of these relationships is strengthened by the fact that the results were consistent through repeated trials during which different strains from representative colonial types were employed. The use of both aerogenic and anaerogenic varieties of this organism permitted a broader basis for challenging the capacity of a drug against a relatively large number of stable colonial variants of this organism. Although it is beyond the scope of this paper to discuss any practical *in vivo* application of the results, it nevertheless indi-

cates that the well-founded ability of an organism to live in more than one phase within a host must be considered before attempting to select a "drug of choice" or to establish optimum levels of drug therapy against a bacterial pathogen.

Our results are basically in agreement with those reported for hemolytic streptococci by Hadley and Hadley (1941). In their study the authors report a greater resistance to sulfanilamide of their smooth and rough phases than that of the mucoid phase. Although our anaerogenic rough (R₂) form was of the same order of susceptibility as both mucoid types, the aerogenic rough (R₁) and both smooth types (S₁ and S₂) were definitely more resistant than the mucoid forms for all drugs tested both with the paper-disc and tube-dilution methods.

The advantage of using wide ranges of drug concentrations (Table I) is manifested by the distinctly greater resistance of S₁, S₂, and R₁ forms at the lower concentrations of antibiotics. Although this relationship generally held at all concentration levels for all the drugs, it was not as marked for penicillin at 26.4 µg per disc, for streptomycin at 1600 µg per disc, and for terramycin at 80 µg per disc. Obviously a more thorough investigation would have to be undertaken dealing with such factors as differences in rate of diffusion of different antibiotics (Patrick *et al.*, 1951) at varying concentrations with the paper-disc method in order to explain the slight deviations noted above.

One of the significant findings in this study is that of the *in vitro* effectiveness of penicillin against *S. schottmuelleri*. The bactericidal effect of penicillin is more pronounced when measured by the tube-dilution - subtransfer method. In Table 2 it can be seen that as little as 5.28 µg per ml was bactericidal for all the colony types after 10 hours' exposure to the antibiotic. These results are in marked contrast to those with chloromycetin, which was comparable in efficiency to pen-

TABLE II
RESISTANCE OF AEROGENIC AND ANAEROGENIC COLONIAL VARIANTS OF
S. SCHOTTMUELLERI TO ANTIBIOTICS AND SULFADIAZINE AS
MEASURED BY THE TUBE DILUTION-SUBTRANSFER* METHOD

Colony Type	Hours of Exposure Prior to Subtransfer	Aureomycin				Chloromycetin				Penicillin				Streptomycin				Terramycin		Sulfadiazine	
		Concentrates in µg per ml				Concentrates in µg per ml				Concentrates in µg per ml				Concentrates in µg per ml				Concentrates in µg per ml		Concentrates in µg per ml	
		200	20	200	20	66	6	200	20	66	6	200	20	200	20	200	20	2000	200		
		Results of subtransfers**																			
M ₁	10	-†	-	+	+	-	+	-	-	-	-	-	-	-	-	-	+	+			
	24	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	+	+			
	48	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+			
S ₁	10	-	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+			
	24	-	-	+	+	-	-	-	+	-	-	+	-	-	-	-	+	+			
	48	-	-	+	+	-	-	-	-	-	-	-	-	-	-	-	+	+			
R ₁	10	-	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+			
	24	-	+	+	+	-	-	-	+	+	+	+	-	+	-	+	+	+			
	48	-	+	+	+	-	-	-	-	+	-	+	-	+	-	+	+	+			
M ₂	10	-	-	+	+	-	+	-	-	-	-	-	-	-	-	-	+	+			
	24	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	+	+			
	48	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+			
S ₂	10	-	+	+	+	+	+	+	+	+	+	+	-	+	-	+	+	+			
	24	-	+	+	+	-	-	-	+	-	-	+	-	+	-	+	+	+			
	48	-	+	+	+	-	-	-	-	+	-	+	-	+	-	+	+	+			
R ₂	10	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	+			
	24	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-			
	48	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-			

*All original tubes (drug + organisms) were negative throughout course of experiment. Approximately 35×10^4 organisms per ml were present in each of the original tubes at the beginning of tests.

**48 hours incubation at 37° C.

† - = no growth; + = growth.

icillin when tested by the disc method, yet proved to be primarily bacteriostatic when evaluated by the tube-dilution - subtransfer method. The claim that *S. schottmuelleri* was inhibited for 18 hours by chloromycetin (McLean *et al.*, 1949) in concentrations of 2.5 µg per ml (serial dilution method—no subtransfers) can therefore probably be interpreted as bacteriostasis, since our data indicate that at a concentration of 20 µg per ml (Table 2) chloromycetin was not bactericidal in less than 24 hours for any of the colonial forms, and only after 24 hours with the susceptible mucoid types and R₂. However, it is recognized that there may exist a difference in susceptibility to the same antibiotic in different strains of the same species.

Since the tube-dilution - subtransfer method affords an opportunity for differentiating between bacteriostatic and bactericidal action, whereas the common practice with the paper-disc method is not to make subtransfers from the clear zones surrounding the disc, it would appear that the former method is better suited for evaluating differences in bactericidal susceptibility of various colonial states of a particular bacterial species. Because of basic differences in the two methods, however, their results are not suitable for exact comparisons.

In a recent paper by Sevag and Rosanoff (1952) the authors discuss the two prevailing major concepts explaining resistance of microbial populations to drugs, i.e., spontaneous mutation, and response to direct

chemical action. In the light of considerable evidence from various sources indicating that bacterial resistance to chemical agents is often associated with particular colonial states of a bacterial species, it seems desirable that another explanation of bacterial resistance be considered.

The natural occurrence of bacterial species in more than one colonial state has been repeatedly demonstrated. The existence of such states has been widely recognized but variously interpreted by different investigators. Some consider these phenomena mutants; others regard them as normal developmental stages (some essential, others incidental) in the life cycle of the bacterial species. Hadley (1937, 1939) has indicated that a bacterial species is the sum total of an orderly relationship of developmental stages ("species microphyte") which are manifested in different colonial phases. The recent work on pleuropneumonia-like organisms has not only indicated the natural relationship of L-type colonies to recognizable parent cultures, but also has shown the L-type colonies of *Streptobacillus moniliformis*, *Hemophilus influenzae*, *Bacteroides*, etc., to possess much greater resistance than the parent forms to such drugs as penicillin (Dienes, 1947, 1948). However, in another paper (Dienes and Weinberger, 1951) it is stated that with *Salmonella typhosa* and *Salmonella typhimurium* the susceptibility is the same for the L-type and the parent colonies. As previously noted at the beginning of this paper,

several other investigators have also shown that different colonial states exhibit different degrees of resistance to specific drugs.

In the light of such investigations and of the results reported in this paper, it seems plausible that some inherent factor in a colonial state may be responsible for the resistance of that state to specific drugs. This possibility also deserves consideration as a possible explanation of bacterial resistance to chemical agents. This does not imply overall resistance of single colonial forms to all drugs (Gainor and Williamson, 1951), but rather suggests that recognizable colonial variants show different demonstrable degrees of resistance to specific drugs and that the degree of resistance for a bacterial species to a specific drug may vary with the colonial state under consideration.

SUMMARY

1. A study of relative resistances of six colonial types representing aerogenic and anaerogenic mucoid, smooth, and rough forms of *S. schottmuelleri* to various antibiotics and sulfadiazine is presented.

2. Marked differences in susceptibility between the various colonial types, when tested both by the paper-disc and tube-dilution - subtransfer methods, were noted. The aerogenic smooth and rough colony types and the anaerogenic smooth form proved to be most resistant, while the mucoid forms and the anaerogenic rough form were most susceptible.

3. Penicillin and chloromycetin were the most effective drugs when tested by the paper-disc method, while penicillin showed greatest bactericidal activity and chloromycetin least activity of the antibiotics when tested by the tube method. Whereas terramycin was more effective than aureomycin when evaluated by the paper-disc method, both were equally efficient when

tested by the tube-dilution - subtransfer method. Streptomycin followed these two antibiotics in efficiency when tested by both methods. Sulfadiazine was the least active drug used in these studies.

4. From our study no exact comparisons of results can yet be made between the two methods of testing.

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GANGRENOUS CHOLECYSTITIS RESULTING IN DEFECT OF THE HEPATIC DUCT; SUBSEQUENT HYPERSPLENISM

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GANGRENE of the gallbladder in the course of acute cholecystitis is a well-known clinical picture and the clinical course usually is very stormy. Unless the patient is operated upon at an early stage of the attack, the gallbladder wall is destroyed by gangrene, its contents spill into the abdominal cavity, with considerable danger to the patient's life. In more fortunate cases the duodenum or some other abdominal organ successfully adheres to the point of threatening perforation, so that the perforation takes place into the adherent organ; if this is a hollow viscus, the perforation effectively drains the gallbladder and the gangrene recedes. Bachhuber (1) reported five deaths in a group of 26 cases of gangrene of the gallbladder; Clifford (3) reported an over-all mortality rate of 34% in a group of 100 cases, and amongst the operated cases in the same group the mortality rate was

28.2%. These reports show that gangrene of the gallbladder represents considerable danger to the patient's life. Even if the patient survives the stage of acute gangrenous inflammation, often a condition persists that requires secondary operation, representing an additional threat to the patient. Such condition may be an internal biliary fistula. Usually there is considerable residual inflammation or fibrosis around the gallbladder and around the fistula. Operative procedures for correction of the fistula are difficult because the residual inflammation or fibrosis destroyed cleavage planes and natural borders. The danger of further injury to hollow viscus organs or bile ducts is also great. The general condition of patients with biliary fistula may be poor due either to the gangrene or to the loss of bile, and in some instances to both. Communication between the gallbladder and the hepatic duct is one of the possible forms of internal

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biliary fistula. It is necessary to differentiate between the congenital anomalies and the fistulas due to perforation caused by disease. The picture of congenital anomalies is complicated. Mentzer (8) studied bile duct anomalies in men by way of comparative anatomy and came to the conclusion that bile duct anomalies in men are found as normal in some animals. Amongst these he found, in some animals, the presence of two hepatic ducts, one of them entering the gallbladder and continuing by way of the cystic duct into the duodenum, the second by passing the gallbladder and emptying directly into the duodenum. He did not mention amongst the duct patterns encountered in his comparative anatomic studies any single hepatic duct entering the gallbladder and continuing by way of the cystic duct. Schachner (10) however, described a specimen taken from the body of a 49 year old man. The excretory apparatus of the liver was so arranged that the whole of the bile must have passed through the gallbladder on its way to the intestine. The gallbladder itself was much smaller than average, and when laid open it measured two inches in length and less than that in breadth. In its upper or attached wall there were two openings, the larger one being the main hepatic duct, the smaller one a cysto-hepatic duct. This anomaly was reported as a congenital one. Schachner (10) also quotes Owens that in wolf-fish (*Erythrus Lepidospiren*) the bile is conveyed to the gallbladder by hepatocystic ducts and thence by cystic duct to the duodenum. In certain reptiles (*Siren Amphiuma*) the anatomy is similar.

There are comparatively few reports of acquired cholecysto-hepatic fistulas. A case was reported from the clinic of DeWitt Stetten (11), in which a large stone protruded from the neck of the gallbladder into the common duct with practical absence of the cystic duct. This case, strictly speaking, is not an internal fistula, but it suggests that widening of the cystic duct by erosion caused by stone may result in a picture of cholecysto-hepatic fistula with absence of the cystic duct; in evaluating some of the case reports quoted below it may have to be considered that some, reported as cholecysto-choledochal fistulas may really be eroded cystic ducts. Behrend and Cullen (2) reported three cases of cholecysto-choledochal fistulae. All three cases presented several features in common:

1. All had long pre-existing chronic cholecystitis.
2. Jaundice was the presenting symptom in each case.
3. Artificial communication was caused through erosion by stone.
4. In each case, in spite of meticulous dissection, it was not possible to identify the cystic duct.
5. Extreme caution had to be exercised not to mistake the common duct for the cystic duct.
6. Since the gallbladder was intimately fused to the common bile duct, complete removal of it would have jeopardized part of the common duct.
7. T-Tube drainage was used from 7 to 12 weeks in the treatment.

Strikingly similar features were present in the case that is the subject of this report.

MAY, 1954

Behrend and Cullen did not find any other case of cholecystocholedochal fistula reported in the literature. Curvoisier (5) reported 8 cases of fistulas between bile ducts amongst 384 spontaneous biliary fistulas. Mirizzi (9) reported 4 cases in great detail; 1 cholecystocholedochal fistula, 1 cholecystohepatic fistula, 1 cholecystohepatico-choledochal fistula, and the co-existence of a cholecysto-hepatico-choledochal fistula and a cholecystoduodenal fistula. Operative cholangiogram was used to identify details and this was a great help in clarifying the situation, confused as it was by results of inflammation and scar formation. At times more than one puncture and injection of contrast material was necessary to obtain full clarification.

HYPERSPLENISM

Hypersplenism is a syndrome and not a single disease. The pathologic processes leading to hypersplenism vary. For purposes of this report a brief resume is given: for details the reader is referred to the quoted literature. The diagnosis of hypersplenism may be made by two criteria:

1. Certain blood elements are reduced, usually in the presence of splenomegaly.
2. Splenectomy corrects the blood picture.

The blood elements in question are: a) red blood cells, b) white blood cells, c) platelets, d) a combination of any two of these or all three. As the second criterion means removal of the spleen, at times this procedure may be done and it is found afterwards that the anemia was not due to hypersplenism. Utmost care has to be exercised because certain anemias may be aggravated by splenectomy; this is particularly true in cases with atrophic bone marrow. As a general rule it may be stated that in cases of hypersplenism the bone marrow is either normal or hyperactive. Bone marrow studies are a guard against poor results of splenectomy. The mechanism of anemia is not fully known, but various mechanisms are suggested. Damask and Welch (6) suggest that some splenic principle affects the blood elements outside of the spleen. This principle inhibits the maturation and delivery of the blood elements. The spleen itself is not the "slaughterhouse" but the "graveyard" of the red cells. Doan's (7) concept inclines to place the actual destruction of blood elements into the hypersplenic spleen. It is possible that at times the first, and at times the second mechanism is operative. Some, but not all anemias caused by hypersplenism are hemolytic. Interesting observations were published (4) regarding these cases. If blood transfusion is given from a normal donor to a recipient with acquired hemolytic jaundice, the survival time of the transfused cells is reduced. The patient with an acquired hemolytic jaundice has a coating antibody on his erythrocytes and this can be shown by Coomb's test; but transfusion of blood from such donor to a normal recipient will be followed by normal survival rate of the transfused red cells. This indicates that the presence of the coating antibody does not necessarily doom the red cells to rapid destruction. The complete mechanism of shortened erythrocyte life span in patients with acquired hemolytic jaundice is not known. If such a patient is transfused with blood found to be compatible by the routine laboratory studies, crisis may occur. This can be prevent-

ed by careful evaluation including special studies for detection of anti-bodies, such as the Coomb's test, the use of bovine albumin as serum diluent, and the use of tripsinized red cells.

There are various classifications of the causes of splenomegaly resulting in hypersplenism. Damashek (6) speaks of idiopathic cases and cases with known cause; Zollinger (12) and his collaborators speak of primary and secondary cases. Apparently idiopathic and primary are the same, so are those of known cause and the secondary. Damashek (6) classifies the splenomegalies as follows:

1. Infectious states.
2. Portal and splenic vein hypertension.
3. Excessive cellular proliferation.
4. Excessive red blood cell destruction.
5. Disorders of lipid cellular metabolism.
6. Primary tumors and cysts of spleen.
7. Idiopathic types.

Splenectomy may be indicated, if:

1. The size of the spleen causes discomfort.
2. If hypersplenic syndrome is present.

CASE REPORT

On June 3, 1952, a 58 year old female patient was admitted by Dr. G. Stayner to the Pearl River General Hospital. Her previous history included an operation for carcinoma of the right breast in 1949. A radical mastectomy was done. Half a year following this operation she became jaundiced but had very little abdominal discomfort. A physician told the patient that she should never permit anybody to operate upon her for the jaundice; he also told one of the patient's sons, that the patient had metastatic cancer of the breast invading the liver. Since then the jaundice waxed and waned, the patient had at times some abdominal discomfort, but no pain. She lost weight. For over a year prior to her hospitalization Dr. Stayner took care of her. He felt that she should be explored but the patient did not accede to this suggestion. On June 3, 1952, she was seized with acute abdominal pain. She was hospitalized immediately for further study. On admission the patient was acutely sick and jaundiced; with considerable rigidity over the abdomen. Blood count on June 3 was: Rbc: 4,230,000; Hemoglobin: 80%; Wbc: 9000; Segmented Neutrophils: 65%; Stabs: 3%; Lymphocytes: 32%; Icteric Index: 40%; Van den Bergh: Immediate direct reaction; Bilirubin: 7.5 mgs; Bile in urine three plus. During the day of June 4th the patient continued to have abdominal pain. During the night from the 4th to the 5th, the patient was seized with excruciating abdominal pain, the abdomen showed board-like rigidity, she vomited. On the morning of June 5th she was operated upon by Drs. Lefkowitz and Stayner as an abdominal emergency. The operative findings as described by Dr. Lefkowitz were: generalized peritonitis, empyema of the gallbladder, with one perforation on the medial aspect, and another perforation on the lateral aspect of the gallbladder; the liver, gallbladder and gastrohepatic ligament very edematous; numerous stones in the gallbladder, some stones free in the peritoneal cavity. The operative procedure consisted of scoping out the stones of the gallbladder. This was followed by marked bleeding from the gallbladder cavity; this was packed through one of the perforations, a drain inserted into the second perforation; another drain towards the foramen of Winslow, and also packing towards that region; Sulfadiazine powder was introduced into the abdominal cavity and the incision closed. The immediate postoperative course was stormy. I saw the patient in consultation with Dr. Lefkowitz and Dr. Stayner on the 11th postoperative day. The patient presented the picture of deterioration. The relevant findings were: jaundice; well-

healed mastectomy scar over the right half of the chest; recent abdominal incision with two abdominal drains, both draining a mixture of bile and pus; diffuse muscular rigidity of low degree. The Nurses' Notes stated that the stools were clay colored. The temperature was near normal. It was decided to prepare the patient for abdominal exploration aiming to re-establish the normal flow of bile and to remove the gallbladder if circumstances permit.

Additional laboratory data obtained after consultation were: Cephalin flocculation 1 plus in 24 hours. Bromsulphalein 5 mgs per kilo dose: 110% in fifteen minutes, 106% in thirty minutes. Prothrombin time 17 seconds, control 16 seconds. It was decided to disregard the bromsulphalein test as obviously incorrect and proceed with the operation.

On the 17th day following the first operation the patient was re-operated. The abdomen was entered. The stomach and the duodenum carefully separated from a fibropurulent mass which on further dissection proved to be the remnant of the gallbladder. Opening into the lumen of the fibropurulent mass and piecemeal dissection around it showed that two ducts entered a cavity in the fibropurulent mass. One of these when probed ran from the abscess cavity into the porta hepatis; on further probing and exposing the porta hepatis it was identified as the common hepatic duct; the junction of the right and of the left hepatic ducts could be seen. There was no evidence of any other hepatic duct found; nor was it possible to see the hepatic artery or to feel its pulsation. By probing the second duct it was found that this led into the duodenum. One gallstone of the size of a bean was removed from this duct. The cystic duct was not identified in spite of meticulous dissection. The liver was carefully inspected and palpated, it appeared normal; there was nothing found indicating carcinoma. The abscess cavity and the fibrous mass were the result of gangrene of the gallbladder which caused a defect of the hepatic duct, and either occluded or destroyed the cystic duct. The operation was continued by resecting most of the fibrous mass, but its posterior part and small flaps of it near the ducts were left in situ. A T-Tube, about one cm. in diameter, was inserted into the hepatic and into the choledochal duct stumps, the fibrous mass flaps closed over the cross arm of the T-Tube. Free flow of bile into the T-Tube was observed after this suture. A wide Penrose was placed near to the duct reconstruction and the abdomen closed. The postoperative course was uneventful. The patient rallied, and vital functions returned to normal within a few days. The long arm of the T-Tube was intermittently occluded starting about 7 days postoperatively. This did not cause any discomfort, and the stools returned to normal color. The jaundice gradually cleared. The abdominal incision healed well. The T-Tube was left in situ for three months, then removed, its site healed within a week. The patient gained weight and strength. The results of the duct reconstruction are excellent up to the date of this report.

Following the complete recovery from the cholecystectomy and duct reconstruction Dr. Stayner noticed that anemia developed, the red blood cells dropped to 2.5 million, it seemed to be a secondary type anemia. Leukopenia was noted also. On October 9, 1952, in consultation with Dr. Stayner an enlarged spleen was found. It reached about 10 cm. below the left rib arch. It was freely movable, not painful. Originally we planned to have the patient hospitalized for purpose of complete study, that would have included spleen and liver needle biopsy. The patient did not agree to this. A limited study was made. By this time the patient received intensive treatment of liver injections and iron by mouth; pernicious anemia would not have been detected by blood count. A sternal marrow aspiration was done; the report on this indicated considerable marrow activity; but megaloblasts and promegaloblasts, which occur in treated pernicious anemia in high percentage, were not reported. This seemed to rule out pernicious anemia. The cephalin flocculation was negative. There was no ascites present, the liver was not enlarged, therefore primary cirrhosis seemed to be ruled out. Resistance of red cells against hemolysis was not determined, liver and spleen biopsies were not done. By the end of November, 1952, the patient receiving liver and iron in large doses, the blood count was: 4,500,000 Rbc's

with good hemoglobin content, Wbc's: 2000; Platelet count: 230,000. Hypersplenism due to splenic vein thrombosis or to chronic infectious splenomegaly were the probable diagnoses. The patient was again operated upon on December 2, 1952 at Pearl River General Hospital. A spleen measuring 25 x 10 x 10 cm. was found and removed with no technical difficulty. The gross appearance of the spleen was not diagnostic; there was no thrombosis found in the veins of the pedicle. The liver again appeared grossly normal; a liver biopsy was taken. The patient made an uneventful recovery and left the hospital on the fifth postoperative day. The removed spleen was examined by Dr. Hobson A. Davis, who gave the following report on the sections: "Several sections prepared for microscopic study. They all show Malpighian corpuscles widely separated from each other. This separation is apparently due to an increase in the size of the sinusoids. The Malpighian corpuscles do not show any characteristic hyperplasia either of the reticulum cells, or the lymphocytes; in fact they are apparently normal. The most characteristic feature in reference to the splenic pulp is the presence of a moderate to large number of eosinophiles associated in some places with slight fibrosis. Many of the sinusoids are distended with blood and there is an apparent hyperplasia of the endothelial cells lining the sinusoids. More careful study also reveals an occasional giant cell. These giant cells are of the foreign body type and certainly do not suggest tuberculosis. "The presence of the giant cells and the numerous eosinophiles caused considerable concern with me as to whether or not this was Hodgkin's disease. It is my final conclusion that the giant cells are not of the Reed-Sternberg type and that this is probably not Hodgkin's disease. I am unable to account for the numerous eosinophiles unless you, as the attending physician, have evidence pointing toward an infectious basis. I do not believe that this is a neoplasm."

The liver biopsy happened to be examined by another pathologist, who found chronic hepatitis with inflammatory and fibrous changes. A detailed history and the findings on the liver biopsy were submitted to Dr. Davis. He then stated that the conclusion is definitely justified, that the splenomegaly was on an infectious basis.

Since then the patient had an uneventful course.

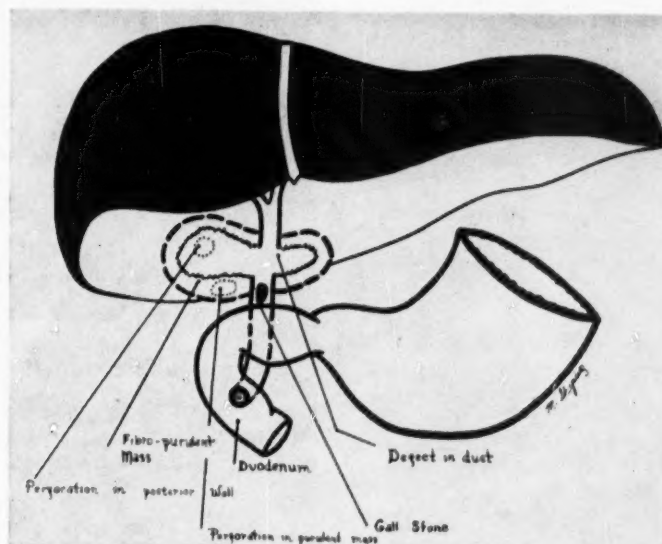
On the 14th of May, 1953, she was re-examined. She gained weight, her appetite is good. She has normal bowel movements, never clay colored. She is not jaundiced. Takes no medication. Laboratory studies show the following: Rbc: 5,120,200; Hemogl.: 16.5 gms.; Color Index: 0.90; Hematocrit: 46% Vol. index: 0.98; Ict. index: 3; Mean red cell

volume: 98 microns; Wbc: 9000; Polys: 54%; Stabs: 2%; Lymphs: 41%; Monocytes: 2%; Eos: 1%; Total protein: 8.1 gms.; Albumin: 5.5 gms.; Globulin: 2.6 gms.; Alkaline phosphatase: 8.5 units (King Armstrong); Thymol turbidity: 0.8 units; Cephalin flocculations: 1 plus in 48 hours. On intensive questioning this time it was brought out, that she had jaundice for perhaps one year, though intermittently, preceding the mastectomy; that for three years prior to the first abdominal operation she felt very full after meals; she does not have this full feeling anymore.

DISCUSSION

The patient obviously had cholelithiasis and choledocholithiasis of long standing; the intermittent jaundice was caused by the choledocholithiasis. However, the jaundice was painless, therefore the erroneous impression arose that the jaundice is due to metastases of the carcinoma of the breast. Investigation of the jaundice was not carried out due to the erroneous diagnosis, that seemed to explain the jaundice. Presence of stones predisposed to further aggravation of the gallbladder disease; acute gangrenous cholecystitis occurred. The destruction caused by it resulted in an abscess and in a defect of the common hepatic duct. The only alternative to this mechanism would be, if a congenital anomaly, similar to the case in Schachner's report as quoted would have existed, where the hepatic duct entered the gallbladder directly and the cystic left the gallbladder, without a second common hepatic duct or cystic duct being present, and then cholelithiasis and later gangrenous inflammation would have set in. No report of an abscess such as reported here was found in the literature. This abscess bore some similarity to the three cases of cholecysto-choledochal fistulae reported by Behrend and Cullen. Five of the common features of those three cases were present in this case, namely:

1. This case had long pre-existing chronic cholecystitis.
2. Jaundice was the presenting symptom for a long time.



Findings on Second Laparotomy
(June 22, 1952)

3. In spite of meticulous dissection the cystic duct could not be identified.
4. Extreme caution had to be exercised not to mistake the common duct for the cystic duct.
5. T-Tube drainage was used for 12 weeks.

One point quoted in the Behrend report, that the fistula was caused by erosion, was different in this case, because this was not a fistula, but an abscess; and it was caused by gangrenous inflammation. Another different point was that in Behrend's cases the gallbladder was intimately fused with the common duct; in this case there was no definite gallbladder present, but the abscess wall was adherent to the common choledochal duct in addition to being adherent to the stomach and to the duodenum. Reconstruction in this case paralleled the type of reconstruction used by Behrend. Whether or not this type of reconstruction resulted in a permanently open good channel for the flow of bile, remains to be seen. Perhaps the fact that a very wide T-Tube was inserted between the loose duct ends and leaving this tube in situ for 12 weeks will result in a permanently good channel. As conditions were when this patient was operated upon, this type of repair seemed to be much preferable to a possible hepaticojejunostomy, or mobilization of the common duct with end to end suture to the hepatic duct. The rise of hypersplenic splenomegaly was a further very unusual complication. Various types of infection were found to produce infectious hypersplenic splenomegaly, but no report was found that acute gangrenous gallbladder disease would have caused it. Infectious nature of the splenomegaly in this case was suggested by the pathologist prior to knowing the history and the operative findings; and stated to be such after full knowledge of the details. The marked clinical improvement of the patient following splenectomy proved that the splenomegaly was a hypersplenic one.

CONCLUSION

A case of long standing painless jaundice is reported. The jaundice was erroneously thought to be due

to metastatic malignant disease in the liver; but it was due to common duct obstruction. Acute gangrenous inflammation supervened causing an abscess and a defect of the hepatic duct. Operative repair resulted in improvement of the biliary duct status, but was followed by hypersplenic splenomegaly. Splenectomy was then done, and this was followed by good clinical improvement.

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EVALUATION OF A NEW METHOD FOR SUPPLEMENTATION OF GASTRIC HYDROCHLORIC ACID*

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REPLACEMENT of the intubation method of gastric analysis by the simplified cation-exchange-indicator-quinine (C.E.I.Q.) urine test has made it possible to investigate the achlorhydric patient more conveniently (1, 2). It now is possible to conduct mass screening surveys to detect achlorhydria and its associated conditions, such as carcinoma of the stomach, pernicious anemia, etc. It provides a precise diagnostic test for evaluating the nonorganic malfunctions directly for the stomach, and indirectly for the intestinal tract.

A new medicine is available which adds hydrochloric acid in quantities sufficient to ensure active digestive

function. Our experience with this medication on 104 achlorhydric patients has shown that the many functional digestive complaints and dietary intolerances have been symptomatically relieved. Our experience with gastrectomized patients who have had cancer of the stomach is limited; however, our preliminary observations have shown that this new medicine possesses the distinct advantage of speeding post-operative convalescence, permitting a more rapid return to a full diet and a faster rehabilitation to a normal condition.

In the past, many variations in the technique of administering hydrochloric acid to the achlorhydric patient have been used. The difficulty of obtaining adequate replacement in the stomach through the use of drops of dilute hydrochloric acid introduced into the

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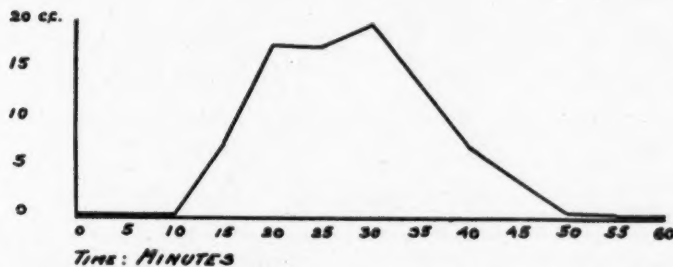


Chart 1: Typical curve of secretion of gastric juice collected at five-minute intervals during the mastication of palatable food.

mouth has long been recognized. Further, that method of medication was distasteful to the patient and caused etching of the teeth. The gelatin capsule which released hydrochloric acid in the stomach overcame some of the difficulties of oral administration. However, the rapid release of relatively large quantities of acid in a short period of time may cause burning and discomfort because the achlorhydric stomach is not well protected by mucinous secretions. In addition, too rapid release may permit an overquick neutralization of the acid before it has served its primary purpose. Because of this, betaine or glutamic acid hydrochloride preparations have not been tolerated in doses sufficient to provide

the amount of hydrochloric acid needed for optimum digestion.

The preparation used in our study* is a material which gradually disintegrates, releasing the hydrochloric acid over a time interval comparable to the physiologic release of the normal stomach. Each tablet contains betaine hydrochloride 440 mg., methyl cellulose 110 mg., and pepsin (1 to 10,000) 32.4 mg., relatively 50% more acid than provided by the gelatin capsule.

The tablet is coated in such a manner as to permit

*"Normacid" provided by Stuart Co., Pasadena.



Fig. 1: Dissolution rate of normacid (Stuart) as visualized roentgenographically. 0 minutes.

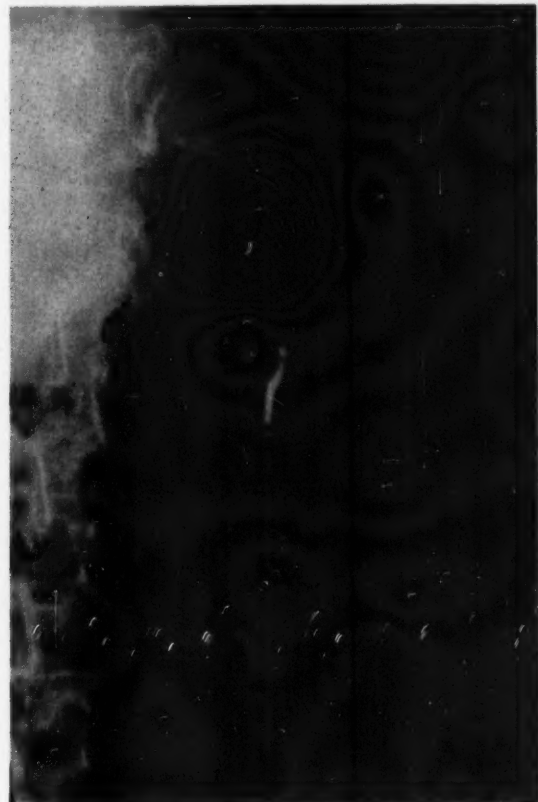


Fig. 2: 15 MINUTES: Tablet swollen; some disintegration at ends.

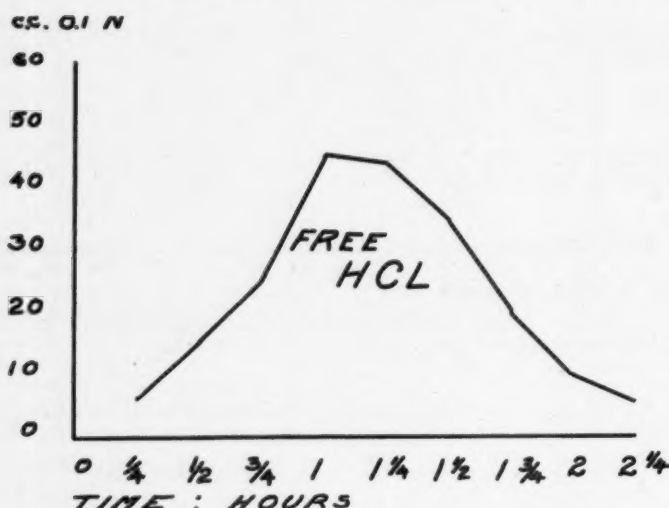


Chart 2: Normal curve of gastric acidity following an alcohol test meal.

its rapid transit into the stomach and its slow dissolution therein. Chart 1 illustrates the time-hydrochloric acid curve of normal gastric functions as plotted from intubation specimens collected at 5 minute intervals during mastication without swallowing palatable food.



Fig. 3: 30 MINUTES: All lower left portion of tablet disintegrated.

Chart 2 shows the normal curve of gastric hydrochloric acid following a 50 cc. 7% alcohol test meal. The interval of normal acid secretion is between 30 minutes and 2 hours and the maximum secretion is in 1 hour.

Figure 1 presents photo-roentgenograms taken at 15 minute intervals after swallowing the new acid tablet in which a barium core had been incorporated to produce radiopacity. The visualization of dissolution in the fasting stomach begins at 30 minutes and is complete at 90 minutes. This is characteristic of the roentgenographic findings in 8 of 10 patients so studied. In 2 cases the tablet failed to remain in the stomach when a test meal* was eaten after swallowing the acid tablet. In each of 12 additional cases where one third of the test meal was consumed prior to swallowing the barium tagged tablet, it was retained in the stomach until complete dissolution occurred. Evidence of dissolution was seen in the 15-minute films in each case. However, the end point of dissolution ranged from 75 to 90 minutes instead of the 60 minute interval noted in the fasting stomach. These rates of disintegration fall within the minimum and maximum time intervals shown by charts 1 and 2. The unpleasant side reactions of earlier techniques of administration are avoided, and at the same time a more adequate level of hydrochloric acid therapy is made possible.

The release of hydrochloric acid in functional amounts was demonstrated in another way. One or more tablets were administered simultaneously with the C.E.I.Q. powder to 5 patients who previously had shown no free hydrochloric acid by intubation, and who had yielded quinine sulphate values of less than 25 micrograms for the one and two hour urine specimens. The quinine sulphate urine values in each case rose to above 50 micrograms for both the one and two hour specimens. These values are above the range

*Test Meal—1. sliced orange, 1 piece lightly buttered wholewheat toast

2. acid tablet

3. 2 soft boiled eggs, 1 piece lightly buttered wholewheat toast, 1 1/2 cups of coffee.

of achlorhydria but are below the range of normal values (100 mg. of quinine recovered per hour).

Owing to the difficulties inherent in collecting total (quantitative) gastric secretions under normal conditions, exact values for the hydrochloric acid content of the normal stomach have not been definitely established. Several rather widely separated ranges of values are found in the literature. One authoritative text (3), however, gives values between 80 and 140 cc. of 0.1 normal hydrochloric acid as the normal range of gastric secretion. The hydrochloric acid content of each of the new tablets has been calculated to yield the equivalent of 30 cc. of 0.1 normal hydrochloric acid.

Our experience with this form of therapy indicates that initial dosage levels, even in true achlorhydria, should be no higher than one tablet with each meal for a period of several weeks. The majority of patients who have been achlorhydric for a long period of time, and who have been receiving no therapy, occasionally experience transient nausea during the first few days of therapy. The dosage may be increased to two tablets (880 mg. of betaine hydrochloride) with each meal after this induction period. Upon occasion the patients find that one tablet early in each meal and one tablet after meals is the most satisfactory plan of administration.

The medication described above was prescribed for 27 patients found to be achlorhydric in a series of tests reported (2) (conducted in order to determine the

validity of the C.E.I.Q. urine test for free hydrochloric acid as compared with the intubation method). An additional 77 patients found to be achlorhydric by the C.E.I.Q. test have been taking this medication. We found remarkable response of the achlorhydric patient to this treatment, even when full consideration is given to the transient boost some patients receive from any new form of therapy. All but 6 of the patients in this group of 104 have reported a general improvement of physical condition and an increase in strength. The benefits to the other 98 cases, however, have not been transient, nor can they be described in terms of psychological lift.

The complaint of indigestion with gas in 34 patients was completely relieved. Many others were relieved of vague discomfort in the epigastrium. The most common complaint, of rawness and soreness of one or more of the oral surfaces, which was mentioned by 87 patients, was relieved entirely in 17 cases and to some extent in 44 more. The objective oral symptoms of superficial inflammation of one or more oral surfaces have shown improvement in all but 16 cases, and nearly complete remission in 12 cases. Extensive vitamin therapy in the past (without recognition of the achlorhydric state) had failed to produce improvement in oral complaints. All patients in our series, however, are being maintained on adequate vitamin supplementation in addition to acid therapy.



Fig. 4: 45 MINUTES: Upper portion still partially intact.
MAY, 1954



Fig. 5: 60 MINUTES: Tablet disintegrated; barium scattered.

Clinical procedures for therapy of achlorhydria were successful and therapy strongly reinforced the validity of the laboratory data concerning the achlorhydric patients tested in this study. We conclude that all patients over 60 years of age who have digestive complaints relative to the epigastrium should be studied for gastric acidity by the C.E.I.Q. test. All those found to have achlorhydria or hypochlorhydria should have immediate roentgenographic studies for possible carcinoma of the stomach. Those who do not have a neoplasm should receive the benefit of this new therapy.

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ABSTRACTS ON NUTRITION

CONRAD, S. W.: *The problem of weight reduction in the obese woman*. *Am. Pract. & Dig. Treat.*, 5, 1, Jan. 1954, 38-47.

It is easy enough to give a fat woman a reducing diet but she may not follow it for any one of many possible reasons. Conrad's analysis of the reasons for resistance to dieting and to losing weight brings up a sheaf of psychological possibilities and he feels that many of the obstacles can be overcome by a superficial psychotherapeutic approach. In short, there is usually some reason, more or less involved, why a fat woman does not desire to lose weight and success depends upon finding that reason. Perhaps only a psychiatrist could do this properly.

VIVANCO AND BARREDA: *Practical results of dietary treatment of arterial hypertension*. *Rev. Espan. Enf. Del Ap. Dig. Nutr.*, XII, 6, 570-581, Nov.-Dec. 1953.

The writers study the practical results of dietary control of arterial hypertension. They review low-sodium and calorie-restriction diets, make some comments on the theoretical bases on which those diets rest and on their efficiency in the treatment of hypertensive patients.

ROCHA, A.: *Contraindication of sugar-free diets in certain cases of diabetes*. *Rev. Espan. Enf. Del Ap. Dig. Nutr.* XII, 6, 581-585, Nov.-Dec. 1953.

The writer sets forth and discusses the bases for contra-indication of diets too low in carbohydrates in patients with diabetes mellitus.

VILLAR CASO, J. Y ZOFFMANN, A.: *Hormonal regulation of the plasmatic proteins: adrenal-cortical influence*. *Rev. Espan. Enf. Del Ap. Dig. Nutr.*, XII, 2, 139-143 Mar.-Apr. 1953.

The writers study the effect of adrenal cortical hormones on the plasma proteins of dog. On the whole they find an increase which appears late, in such proteins. At the same time they study the behaviour of the bone marrow in the animals thus treated and observe an increase in normoblasts and decrease in neutrophils and plasma cells.

SHELDON, J. H.: *The clinical spectrum of obesity*. *Brit. Med. J.*, Dec. 26, 1953, 1402-1404.

The usual cause of obesity is an excess of caloric intake over expenditure, a process in which excessive

appetite plays the most important role. Animal experimentation shows that damage to certain nuclei in the medial hypothalamus produces a voracious appetite with weight gain. Destruction of the lateral nuclei, however, may produce a fatal anorexia. Maternal obesity, when it occurs, begins after the birth of the child, reaching a reduced but steady gain in weight after about one year. This type of obesity closely resembles that of rats in whom the hypothalamus has been injured. The weight is finally composed of as much as 60 percent of the entire body in fat. It must be assumed that hypothalamic damage is operative in maternal obesity. Strangely, the birth of a baby boy is four times as likely to produce maternal obesity as the birth of a girl baby, a fact which suggests the operation of an emotional factor. The growth hormone probably is operative in adolescent obesity and perhaps also in maternal and menopausal obesity. The adrenal cortex no doubt is involved in many cases of obesity, particularly those cases showing *striae distensae*. Adrenal steroids may indeed affect the hypothalamus, as obesity may accompany suprarenal tumors.

RODRIGUEZ-MOLINA, R.: *Fundamental concepts in the diagnosis of sprue*. *Ann. Int. Med.*, 40, 1, Jan. 1954, 33-41.

Sprue is now accepted to be a deficiency state amenable to replacement therapy with liver extract, folic acid, folinic acid and vitamin B₁₂ in addition to a high protein, high vitamin, low fat diet. Tropical and nontropical sprue (idiopathic steatorrhea) are believed to be phases of one disease entity. However, nontropical sprue may be imitated by diseases which interfere with the absorption of fat and water-soluble vitamins, e.g., abdominal Hodgkins, lymphosarcoma of the mesentery, amyloid disease, intestinal lipodystrophy and tuberculosis. The diagnosis of sprue depends on the following criteria,—insidious onset, chronicity of symptoms, and paucity of spontaneous remissions; presence of stomatitis and glossitis (but without cheilosis); dyspepsia, diarrhea and steatorrhea; recent weight loss with weakness; free HCl in the stomach in over 90 percent of cases; the presence of a macrocytic, hyperchromic anemia associated with a megaloblastic marrow; a flat glucose tolerance curve (oral); absence of neurological manifestations in the majority of cases; hyperpigmentation of the skin, particularly face, arms and legs; and atrophy of the gastric and rectosigmoid mucosa.

The disease is caused by a change in the small bowel

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physiology, which, in turn, is believed to be secondary to malnutrition.

SINCLAIR, H. M.: *Assessment and results of obesity*. Brit. Med. J., Dec. 26, 1953, 1404-1407.

Reduction in weight lowers mortality in overweight persons, and various disorders that are commoner in the obese can be diminished by slimming. Increased dietary fat (but not increased dietary cholesterol) tends to raise the serum cholesterol level and to produce arteriosclerosis. Obesity is satisfactorily estimated by the thickness of a skin-fold. Overweight and obesity are not synonymous. Muscular persons may be heavier than fat persons and yet they may have much less body fat.

CALLENDER, S. T., TURNBULL, A. AND WAKISAKA, G.: *Estimation of intrinsic factor of Castle by use of radioactive vitamin B₁₂*. Brit. Med. J., Jan. 2, 1954, 10-13.

The absorption of vitamin B₁₂ was assessed by measuring the radioactivity in the feces after oral administration of 0.5 micrograms of vitamin B₁₂ labelled with CO⁶⁰. In 10 patients with normal hematological findings a mean of 31.0 percent (standard deviation of 6.9 percent) of radioactivity in the test dose was recovered from the feces. In 13 patients with pernicious anemia, a mean of 88.7 percent (standard deviation 6.8 percent) was recovered. Sources of intrinsic factor given with radioactive vit. B₁₂ to patients with per-

nicious anemia reduced greatly the percentage of the test dose recovered.

HALSTEAD, B. W. AND LIVELY, W. M.: *Poisonous fishes and ichthyosarcotoxin*. U. S. Armed Forces M. J., V, 2, Feb. 1954, 157-175.

Poisonous fishes, which are endemic to all warm seas, constitute a serious hazard to military personnel. Numerous outbreaks of intoxications and death involving military persons have been reported. Ichthyosarcotoxin is comprised of 4 clinically distinct types: tetraodon, gymnothorax, scrombroid and ciguatera. They appear to vary in severity, types of symptoms, and species of fish. The disease can be defined as a type of intoxication resulting from the ingestion of a neurotoxin which is present in the bodies of certain fishes, and variously manifested by symptoms of extreme weakness, malaise, pruritus, myalgia, paresthesias of the mouth and extremities, paralyses, and convulsions, generally associated with such gastrointestinal symptoms as nausea, vomiting, diarrhea and abdominal pain. Death, when it occurs, is from respiratory paralysis. The treatment is symptomatic. A poisonous fish cannot be recognized by its appearance. The public health and military significance of this disease is grossly underestimated. The same fish may or may not be toxic at a given place or time. The puffer is the most regularly poisonous fish, and in some cases of puffer poisoning, death may occur within 1 to 24 hours after eating it. This is the most violent and serious type of ichthyosarcotoxism known.

EDITORIAL

STANDARDIZATION AND COMMON SENSE

While it is true that the greatest advances in medicine have resulted from important scientific discoveries, it is equally true that success in the treatment of disease still depends upon the sagacity of the individual physician. Analytic methods produce discoveries, but synthesis is required before these discoveries can be effectively applied. Today, general practitioners are becoming a little more scientific and specialists are beginning to be a little more "general" in their attitudes. The one element which has been somewhat sadly neglected by our profession is common sense. In fact, it is not easy to find an internist, for example, who combines vast, detailed knowledge with the saving grace of ordinary intelligence.

The drift toward standardization, particularly in treatment, is as obvious as it is foolish. For example, there is no use in treating peptic ulcer by strict diets, reformation of bad habits, and the use of modern drugs which block the vagus, if the patient's situation is one of frustration. That is why some patients who failed to improve under "specialists" got better fast after consulting their own family doctor, who was

well acquainted with the causes of the stress affecting the patient. The sagacity of the general practitioner showed him the urgent necessity of correcting the irritating factors. Possibly we have all seen ulcers get better when the life situation of the patient became more pleasant.

There is something stupid, for example, in treating the blood sugar of a diabetic patient, instead of the patient himself. It is common to encounter diabetics who feel better immediately when slightly more latitude in diet and insulin is permitted.

What is the sense in forbidding all salt to a person who has a moderate angina, or even an early congestive failure? Loss of appetite soon deprives these individuals of the single pleasure they have left.

Life has not been appreciably prolonged or rendered more livable by modern medical standardization. A wide-angle view of patients and their ailments is sorely needed. It is only the wise physician who knows when to tighten up restrictions and when to ease them. This kind of genius does not seem to be an integral part of medical training, but is rather a personal attribute.

BOOK REVIEWS

PEPTIC ULCER. C. F. W. Illingworth, Williams and Wilkins Co., Baltimore 2, Md., 1954, \$8.50.

This is an unusually thoughtful monograph. The author takes nothing for granted and "uses his head" in all his arguments. For example, his refutation of acid as the cause of pain in ulcer is quite convincing. He does not accept as fact that cigarette smoking makes ulcers worse because a survey of a large number of cases indicated no difference in progress between smokers and non-smokers. He also "debunks" some of the ideas of stress as a cause of ulceration, and holds that people were always under stress. The one telling point is the difference in incidence among African and American negroes. Nutritional factors may indeed be important etiologically. He is doubtful if psychological stimuli affect gastric secretion. He thinks there is such a thing as "the ulcer personality." He does not believe that sudden stress tends to cause perforation or hemorrhage. The section on x-ray diagnosis is unusually brief, but sufficient. Medical treatment might obtain better results if the food we eat was not so extensively "processed." A large section of the book is devoted to surgical treatment.

RAT QUALITY: A CONSIDERATION OF HEREDITY, DIET AND DISEASE. W. E. Weston et al. The National Vitamin Foundation, Inc., 15 East 58th St., New York 22, N. Y., Nov. 1953. \$2.50.

Although rats have been used for many years in nutrition work, the various "strains" of rats are not well known. Stock and purified diets still present many problems. The present volume embraces growth criteria, chronic respiratory infections in the albino rat, the development and use of inbred strains, problems in breeding for quality, genetic and nutritional factors influencing uniformity in laboratory animals, the evaluation of commercial and semi-purified diets as stock

rations and other features. The book is of tremendous value to research workers using rats.

ATLAS OF EXFOLIATIVE CYTOLOGY. George N. Papanicolaou, M.D., Ph.D., Harvard University Press, Cambridge, Mass. 1954. \$18.00.

The chief clinical interest in exfoliative cytology lies in the early detection of cancer. The cytology of exfoliated cells differs from other branches of cytology because desquamated cells undergo degenerative changes and thus acquire specific morphological characteristics. The present volume is in loose-leaf form to permit additions during the fast growth of this new science. It contains 36 plates in color. The colored drawings included in 24 plates are the work of the well-known artist Hashime Murayama, an expert in this type of work. Twelve plates of photomicrographs have been included. The text is brief, but gives an excellent resume of how to prepare slides and make a diagnosis. This is an admirable volume. Through its use, any physician accustomed to microscopic work would eventually be capable of forming a fairly accurate idea as to the malignancy or innocence of a smear.

BOOKS RECEIVED

EXPERT COMMITTEE ON LEPROSY, FIRST REPORT. World Health Organization, Technical Report Series No. 71. W. H. O. Palais des Nations, Geneva, 20 cents.

EXPERT COMMITTEE ON BILHARZIASIS, FIRST REPORT. World Health Organization, Technical Report Series, No. 65. W. H. O. Palais des Nations, Geneva, 30 cents.

GENERAL ABSTRACTS OF CURRENT LITERATURE

CREGAN, J., DUNLAP, E. E. AND HAYWARD, N. J.: *The bacterial content of human small intestine in disease of the stomach*. Brit. Med. J., Dec. 5, 1953.

In cases of disease of the stomach presenting for operation, the small intestine was found to contain only a sparse transient population, irrespective both of gastric acidity and of the degree of contamination of the stomach. It is deduced that the small gut has an antibacterial mechanism which is independent of the gastric germicidal barrier.

SINGLETON, E. B.: *Lesions of the esophagus in infants and children*. Texas State J. M., 49, 12, Dec. 1953, 855-864.

Singleton describes the following conditions which may be demonstrated in children by x-ray—esophageal atresia with or without fistulous communication with

the trachea; tracheo-esophageal fistula without atresia of the esophagus; congenital stenosis of the esophagus; cardiospasm (achalasia); relaxation of the cardia (chaliasia); congenital short esophagus with associated hiatus hernia; anomalous development of the vessels arising from the aortic arch and resulting in pressure deformities. Since the surgeon today can repair most of the defects mentioned, their early diagnosis has become more important.

ANDREW, R. AND ROLLO, A. J.: *The effect on gastric acidity of "nulacin" tablets*. Med. J. Australia, Nov. 28, 1953, 823-24.

Six patients with duodenal ulcer were treated with "Nulacin" tablets which were sucked throughout one hour of an alcohol test meal, and the results compared with those obtained from an alcohol test meal on the

AMER. JOUR. DIG. DIS.

same subjects when no tablets were used. There was a striking reduction in gastric acidity when the tablets were used, especially after the first 45 minutes of the test. The tablets contain whole milk solids combined with dextrans and maltose 40 grains; magnesium trisilicate 3.5 grains; magnesium oxide 2.0 grains; calcium carbonate 0.5 grain and oil of peppermint.

BARRETT, A. A.: *Duodenal ulcer in military personnel*. A social service study of 40 cases. U. S. Armed Forces Med. J., IV, 12, Dec. 1953, 1693-1702.

Adjustment, stress and motivation are all significant factors to be considered in the evaluation of ulcer patients and in determining their proper disposition. Separation from military service through psychiatric channels would seem the proper course when personality factors and faulty social adjustment make it likely that the patient will be an ineffective soldier.

The diagnosis of an ulcer seems related more frequently to stress arising in the personal life of the patient than to that arising in the military service. One of the most conspicuous results of this study was the failure to detect the so-called "typical ulcer personality" in 75 percent of the patients. Patients with a history of poor social adjustment were predominantly non-volunteer soldiers and had very little service. Among volunteers, with satisfactory social adjustment, activation of the ulcer followed a rather obvious emotional or situational stress. Only seven of the 40 had had ulcer symptoms before entering the service.

EISENSTADT, H. B. AND ELSTER, B. B.: *Diagnostic problems of simple gastro-duodenal ulcer*. Amer. Pract. & Dig. Treat., 4, 12, Dec. 1953, 821-827.

The authors discuss most of the diagnostic difficulties in peptic ulcer, but their main emphasis is upon the use of compression films for revealing niches and craters which usually are not seen in films made without compression.

SLOAN, R. D., STAFFORD, E. S., SINGEWALD, M. L. AND SINN, C. M.: *Meckel's diverticulum*. Am. J. Roentgen., Rad. Ther. and Nuclear Med., 71, 1, Jan. 1954, 64-75.

Meckel's diverticulum is present in 1 to 2 percent of the population at large with a 3 to 1 ratio in favor of males. Actually the diverticulum seldom gets into trouble. Hemorrhage, obstruction, intussusception and acute inflammation are the chief pathological complications and these are most likely to occur in the first decade of life. It is relatively unusual to demonstrate Meckel's diverticulum by x-ray. In acute cases a barium enema may be used to reduce intussusception, and occasionally some barium entering the ileum may show up the diverticulum. In cases of bleeding it is justifiable to do a small bowel series, but even this seldom is successful. Two cases are reported in which the diverticulum was successfully demonstrated by x-ray.

ROSS, F. G. M.: *Pyloric stenosis and fibrous stricture of stomach due to ferrous sulphate poisoning*. Brit. Med. J., Nov. 28, 1953, 1200-2.

A previously healthy boy, aged 17 months, swallowed between 6 and 12 tablets of a proprietary preparation of compound ferrous sulphate. This was followed

by vomiting and hematemesis. In less than 2 months pyloric stenosis occurred, also a fibrous stricture of the stomach. Death was due to acute peritonitis following jejunostomy. Compound ferrous sulphate tablets consist of ferrous sulphate Gr. 3, copper sulphate Gr. 1/25 and manganese sulphate Gr. 1/25. Ferrous sulphate is the lethal agent and is converted in the stomach to ferric chloride.

DUNLOP, D. M. AND SIMPSON, S. L.: *Discussion on the diagnosis and treatment of Addison's Disease*. Proc. Roy. Soc. Med., 46, 7, July 1953, 565-571.

Two-thirds of a series of 62 cases of Addison's Disease had systolic blood pressures between 90 and 110 and diastolic pressures between 60 and 70. Anorexia and nausea occurred in 80 percent of the cases. Abdominal pain was an ominous symptom usually heralding the onset of crisis. Most of the untreated cases were hypoglycemic in the morning, making it hard to arouse them from sleep. The only non-clinical investigation needed was routine x-ray of the chest and abdomen. Unusual pigmentation of the skin was present in all but one case. The Robinson-Power-Keppler test, the estimation of the urinary 17-ketosteroids, and the insulin sensitivity test were all useful.

The story of prognosis fell into 4 well defined eras. The first lasted from 1849 (when the disease was recognized) till 1930. In 1930, Swingle and Pfiffner obtained a potent extract of the adrenal cortex. Loeb emphasized the value of salt. From 1930 to 1939 was the "era of cortical extract and salt." The third era was that of desoxycorticosterone acetate (synthesized by Steiger and Reichstein and made available for injection and implantation in 1939). The years 1939-1951 were the D.C.A. era. Since cortisone has become available, a fourth era has begun, that of cortisone and D.C.A. The prognosis was greatly improved with each successive era. A greater knowledge of the use of cortical extract and intravenous fluids in crisis contributed to the improved results obtained by D.C.A. During the past 2 years, out of 16 patients treated by Cortisone and D.C.A., none have died.

The thyroid gland in Addison's Disease may be atrophic. Acute suprarenal insufficiency (crisis) may develop in a person not known to have the disease. Spontaneous recovery may occur in Addison's Disease. The sedimentation rate may be increased without obvious infection. *Physiological doses* of cortisone (12.5 to 25 mg. daily) do not cause spreading of tuberculous lesions but continued *large doses* tend to do so.

Hypoglycemic episodes are not uncommon, and are sometimes fatal. Salt is still useful. In the implantation of DOCA pellets great care is needed to gauge the dose. Overdosage causes salt retention and fluid retention with increased potassium excretion. The latter may lead to muscular paralysis, even myocardial paralysis. Patients treated with DOCA, with or without salt, do not do too well, the carbohydrate metabolism being particularly at fault (hypoglycemia). Cortisone in physiological doses abolishes hypoglycemia, and cortisone is the logical treatment of the disease. Yet added salt and even DOCA may also be required. Cortisone works in crisis but if it cannot be swallowed, intravenous glucose is needed while the injected cortisone is being slowly absorbed. For injection, about 100 mg. a day for several days are required.

YOKOGAWA, M., WYKOFF, D. E. AND RITCHIE, L. S.: *Mass treatment of endamoeba histolytica carriers*. U. S. Armed Forces Med. J., IV, 12, Dec. 1953, 1776-77.

It is generally believed that 10 percent of the Japanese harbor *E. histolytica* and that most of these carriers are asymptomatic. 241 carriers were selected for treatment. One week of carbarsone followed by one week of chiniofon, resulted in a disappearance of the organism in over 99 percent when examined five weeks after treatment. This represents a high level of therapeutic efficiency. In a Matsusawa village prior to treatment, 28.8 percent showed the organism and 8 months later, following treatment, only 4.1 percent were positive. Ultimate benefit from mass treatment will depend on how quickly reinfections occur.

LUBERT, M. AND KRAUSE, G. R.: *Upright cholecystography using the fluoroscopic spot-filmer with graded compression*. Radiology, 61, 6, Dec. 1953, 879.

Using full doses of modern opaque media and following routine prone films, the patient is stood upright behind the fluoroscopic spot-filmer, and varying degrees of compression are used while making a series of spot exposures. For average patients the exposures are 0.1 to 0.2 second at 65 to 75 KV and 100 ma. By such a method stones may often be visualized whereas they were missed in the routine prone films.

WAUGH, J. N., WALTERS, W., GRAY, H. K. AND PRIESTLEY, J. T.: *Annual report on surgery of the biliary system and pancreas for 1952*. Proc. Staff Meet., Mayo Clin., 28, 26, Dec. 30, 1953, 765-768.

Malignant disease was the commonest surgical condition affecting the pancreas, and 60 operations were performed for this disorder. In 22, exploration only was done. In 36, palliative procedures such as cholecystojejunostomy, cholecystogastrostomy and choledochoduodenostomy with or without gastroenterostomy were done. In only two patients was the lesion early and small enough to warrant radical pancreato-duodenectomy.

Cancer of the gallbladder was observed five times. If the lesion is resectable, the gallbladder should be removed *in toto* with a wide wedge of underlying liver.

In benign lesions of the gallbladder and ducts, jaundice more than doubles the risk of operation. Operative cholangiograms were not used routinely inasmuch as their interpretation can at times be misleading.

GRACE, W. J.: *Life stress and gastro-intestinal diseases*. Am. Pract. & Dig. Treat., 4, 12, Dec. 1953, 848-852.

Grace reviews some of the scientific evidence now available to indicate that there is a definite relationship between stress (moods, emotions) and the functional activity of the stomach and intestines. He recommends a careful biographical recording of each patient's experiences, particularly at the time when his first symptoms appeared. Such a biography may require from one to ten hours' interview.

GRAY, H. K., WALTERS, W., PRIESTLEY, J. T. AND WAUGH, J. M.: *Report on surgery of the stomach and the duodenum for 1952*. Proc. Staff Meet. Mayo Clin., 28, 26, Dec. 30, 1953, 757-765.

During 1952 vagotomy alone was not used in the treatment of gastric or duodenal ulcer. It was done on 17 patients, 13 of whom had recurring ulcers after previous gastric operations, and was done as a simultaneous procedure with gastroenterostomy on 27, with partial gastrectomy on 9 and with other procedures on 3. Vagotomy was performed in 33 cases for duodenal ulcer, in 1 case for gastric ulcer and in 16 for stomal ulcer.

A total of 1090 patients was operated on for lesions of the duodenum and stomach with a hospital mortality of 2.6 percent. Of 131 who underwent partial or total gastrectomy for malignant lesions, 4.6 died in the hospital. The hospital mortality for partial gastrectomy for cancer of the stomach was 1.0 percent. In 408 persons having partial gastrectomy for duodenal ulcer, the hospital mortality rate was 1.5 percent.

JONES, J. D. T.: *Treatment of irreducible intussusception*. Brit. Med. J., Dec. 12, 1953, 1304-1306.

Jones presents 91 cases of intussusception occurring in infants and young children. 82 of these were reduced at operation without a single mortality. Nine cases were irreducible and were treated by a two-stage operation of resection and early restoration of bowel continuity with one death. The two-stage operation causes less shock to the infant, and the one-stage operation gave poor results for that reason. There is a possibility of ischemic changes occurring in the outer layer of the intussusception in late cases.

BOCK, D. G., ROSENAK, B. D. AND MOSER, R. H.: *Bleeding from peptic ulcer: a review of 327 cases*. J. Indiana State Med. Assn., 47, 1, Jan. 1954, 41-47.

A review of mortality from bleeding peptic ulcer in three hospitals in Indianapolis, showed a considerably more favorable mortality rate in one hospital as compared with the other two. The reason seemed to be that in the hospital enjoying the lowest rate, patients on admission were seen by staff members, as opposed to house physicians in the other hospitals. Furthermore, the use of blood transfusions was less restricted. Prompt feeding is indicated in the patient with bleeding peptic ulcer, if not in shock or vomiting. Special emphasis is placed on liberal and repeated blood transfusions. If surgery is done, it should be within the first 48 to 72 hours of active bleeding. After 72 hours, best results are obtained by continued transfusions.

HASHEMIAN, H. AND MURRAY, E. T.: *Complications of Meckel's diverticulum*. Brit. Med. J. Mar. 6, 1954, 556-558.

An analysis of 18 cases of Meckel's diverticulum indicates the following possible complications,—diverticulitis with or without perforation, ulceration or hemorrhage or both from heterotopic gastric tissue, intestinal obstruction, umbilical fistula, neoplasms, and foreign bodies. In every case where a Meckel's diverticulum causes symptoms it should be removed.

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GASTRO-INTESTINAL DISTURBANCES

The field of industrial medicine offers "exceptional opportunities for observing the early and initial manifestations of diseases" and of evaluating the efficacy of symptomatic relief, according to Dr. Frank W. Barden, Dr. Paul S. Hill, Dr. William F. Mahaney and Dr. Kenneth J. Cuneo of the Medical Department of the Saco-Lowell Shops and the Webber Memorial Hospital, Biddeford, Me.

"Gastrointestinal disturbances were the chief complaints of more than fifty percent of all patients," report these physicians in the *Maine Medical Association Journal* (45: 11-12, 1954). They believe that "natural belladonna alkaloids are still predominantly the drugs of choice for effectiveness, safety and economy."

In summarizing their report, the researchers state that Donnatal (Robins), a combination of natural belladonna alkaloids with phenobarbital, was found particularly effective for the relief of pain associated with smooth muscle spasm of the gastrointestinal tract, and that more than 85% of the patients with epigastric pain and discomfort were rapidly and completely relieved of symptoms.

Donnatal®, a product of A. H. Robins Co., Inc., Richmond, Va., effected not only a marked reduction in absenteeism, but enabled some employees to resume work within an hour, and subsequent check-ups showed that the patients remained free of symptoms.

ALL THREE TYPES OF POLIOMYELITIS VIRUS SHOWN IN PURIFIED FORM BY PARKE-DAVIS VIROLOGIST

Atlantic City, N. J., April 13.—Purified cultures of all three types of poliomyelitis virus were shown here recently by a Parke, Davis & Company scientist in highly magnified electron-microscope pictures.

Dr. A. R. Taylor, research virologist for the pharmaceutical firm, made the presentation at the meeting of the American Association of Immunologists, held in connection with the Federation of American Societies for Experimental Biology.

His paper, "Electron Microscopic and Ultracentrifugation Studies

on Purified Tissue Culture Poliomyelitis Virus Strains," was accompanied by slide films showing the purified virus of all three types—Mahoney, M.E.F. 1, and Saukett.

Dr. Taylor said this presentation augmented the work he reported last fall, when photographs of the Mahoney strain were shown.

One significant factor in the new study, Dr. Taylor pointed out, was that for the first time scientists were able to grow poliomyelitis virus in high enough concentration to show the virus directly in crude tissue culture.

Purification of the virus, which is grown in monkey kidney tissue, is done by means of ultrafiltration and by sedimentation in an ultracentrifuge that rotates at 40,000 revolutions per minute. The material is sedimented twice in the ultracentrifuge.

Dr. Taylor said the study showed that the size of each Mahoney (Type 1) and Saukett (Type 3) poliomyelitis virus was approximately 33 and 31 millimicrons, respectively, while the M.E.F. 1 (Type 2) strain was somewhat smaller. One millimicron is equal to 1/25,000,000 of an inch.

The Parke-Davis scientist said the results of this work would enable the virologists to study the fundamental chemical and physical properties of all three strains of the poliomyelitis virus together, thereby aiding the overall program to eliminate poliomyelitis.

Associated with Dr. Taylor in the paper were Dr. F. D. Stimpert, director of microbiology; Dr. I. W. McLean, Jr., assistant director of microbiology; and Dr. A. E. Hook, virologist.

NOTICE

Chicago.—The 1954 convention of the National Society for Crippled Children and Adults, the Easter Seal Society, will be held Nov. 3-5, at the Statler Hotel, Boston, it was announced recently by Lawrence J. Linck, executive director.

Convention sessions now being planned will be geared to the overall theme of rehabilitation, with general sessions, institutes, seminars, workshops and roundtables on various specialized subjects, Mr. Linck said.

According to Parker Trowbridge

of Boston, National Society trustee and convention committee chairman, hundreds of delegates to the sessions will make group vacation tours within the two-week period before the meeting begins.

"Under this novel plan for convention delegates," said Mr. Trowbridge, an investment banker, "many people will be able to see for the first time the splendid work of New England's Easter Seal Societies. They will also see the historic sections of the East in their most brilliant, fall colors."

In this 31st national convention of the Easter Seal Society, authorities in every area related to helping the crippled will participate. The 1954 convention will highlight the latest thinking and the newest practical developments in the various fields of work with the crippled. A traditional feature will be the Handicapped Panel, comprising persons who have successfully overcome major handicaps to lead useful lives.

The Easter Seal Society, the oldest and most comprehensive organization of its kind, extends 874 specific services and facilities to thousands of crippled persons each year. It does this through the efforts of 1,253 affiliates in the 48 states, the District of Columbia, Alaska, Hawaii and Puerto Rico.

ALEVAIRE AND OXYGEN CALLED AID IN RESPIRATORY ILLS

Oxygen therapy and the wetting agent Alevaire have immediate value in providing an "efficient tracheobronchial airway" in major pulmonary disorders, according to Drs. Max S. Sadove, Lloyd A. Gittelsohn, Gordon M. Wyant and Paul H. Holinger.

They report on ways to maintain effective respiratory functions in various medical and surgical conditions, in an article in *American Practitioner* (5:11, Jan. 1954).

Noting that obstructions in the respiratory tract affect functioning of the lung, the doctors state that proper treatment aids recovery, avoids complications and saves lives. In surgical patients, preoperative cleansing of the tracheobronchial tree by the patient himself is essential. Oxygen plays "an essential role in treating primary or secondary pulmonary problems,"

and should be humidified by nebulization.

Observing that wetting agents are proving valuable in therapy, they add "we have found Alevaire most useful, and it is probably indicated in all cases where oxygen is administered in the presence of secretions."

Other treatment measures suggested are pharyngeal care, the endotracheal technique and bronchoscopy. Referring to tracheotomies, the group mentions early use of the procedure "as a solution to continu-

ous accumulation of pulmonary secretions."

The International Academy of Proctology will present Gold, Silver and Bronze Awards and Certificates to the three most outstanding world proctologists each year beginning with its 1955 Annual Meeting, Dr. Donald C. Collins, President of the Academy, announced today.

First presentations will be made at the Academy's Seventh Annual

Meeting, which will be held in New York City next April.

At the same time, the Academy's meeting at the Palmer House, Chicago, Illinois, also voted three three-year Fellowships in Coloproctology worth \$1,000.00, \$900.00 and \$800.00 apiece, to be awarded annually to three outstanding medical institutions.

The Jersey City Medical Center, Jersey City, N. J., has been selected as the eastern site for the 1954 award. One of the medical centers in Chicago will undoubtedly receive the midwest award, and a California institution will be granted the far west Fellowship.

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The combination of para-aminobenzoic acid with a low dosage of cortisone "has proved to be a useful method for the clinical suppression of rheumatoid arthritis with the advantage of relative safety," Dr. Leon L. Wiesel and Dr. A. Sidney Barritt of the Brooklyn Hospital report.

Thirty of 31 patients maintained on this regime for a year or more showed improvement comparable to that obtained with a much larger dose of cortisone acetate administered alone, the physicians found. In the combined therapy, 37.5 mg. of cortisone was given orally in three divided doses, an amount "so small that in itself it has proved completely ineffective."

None of the serious side effects observed with the usual doses of cortisone was encountered, the authors state.

Sodium and potassium para-aminobenzoate used in the study were provided by the A. H. Robins Co., Inc., Richmond, Va. Control periods were instituted at intervals by withdrawing PABA until the signs and symptoms of rheumatoid arthritis increased in severity. PABA appears to increase the anti-inflammatory action of a given dose of cortisone acetate two to threefold, the investigators believe.

The study is reported in *The American Journal of the Medical Sciences*, (227:74, 1954). Dr. Wiesel, in the same issue, p. 80, reports experimental *in vitro* findings on the effect of PABA on cortisone metabolism. Although cortisone is rapidly metabolized by liver tissue, this degradation, he



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1. Rowen, B. R., Bachrach, W. H., Halsted,
J. A., and Schapiro, H.: *Gastroenterology*
24:86, 1953.

2. Rogers, M. P., and Gray, C. L.: *Am. J.
Digest. Dis.* **19**:180, 1952.

3. Schaub, K.: *Praxis* **41**:1073, 1952.

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found, is markedly interfered with when para-aminobenzoic acid or its salts are added.

PUBLICATION ANNOUNCED OF THREE SCHERING AWARD-WINNING PAPERS

Fulfilling the major objective of the Schering Award, which is to encourage research and reporting by medical students, the three award-winning papers of 1952 have recently been published in medical journals.

The Journal of the American

Geriatrics Society has published Edward Allen Jones' paper, "Steroid Hormones in Geriatrics" (February 1954). Mr. Jones was a sophomore at Meharry Medical College in Nashville, Tenn., when he won a \$500 first prize.

California Medicine (December 1953) has published the paper by William H. Spencer, then a junior at the University of California School of Medicine in San Francisco. He wrote on "Chemotherapy of the Eye."

The Journal of the Student

American Medical Association published in its March issue the paper by Seymour Cohen, M.D., who was a senior at the State University of New York College of Medicine at Syracuse when he won an Award. His paper was entitled "Topical Uses of Antihistamines," dealing with skin allergies. Dr. Cohen is now at Grasslands Hospital, Valhalla, New York.

Each year, Schering Corporation, pharmaceutical manufacturers of Bloomfield, New Jersey, grants \$500 awards for the best paper on each of three subjects and three \$250 prizes. The 1953 winners have recently received their awards, and subjects for the 1954 competition have been announced.

PARKE, DAVIS & CO. REPORTS NET EARNINGS OF \$2,002,996 AND NET SALES OF \$26,268,175 IN FIRST QUARTER

Detroit, April 27.—Parke, Davis & Company today reported net earnings of \$2,022,996 in the first quarter of this year after payment of United States and foreign taxes totalling \$2,198,000.

The net earnings equalled 41 cents on each of the 4,894,900 shares of common stock outstanding and compared with \$2,209,957 in the first quarter of 1953, or 45 cents a share.

The world-wide pharmaceutical firm also reported net sales of \$26,268,175 in the first three months of this year, compared with \$28,195,757 in the same period of 1953.

On April 30, Parke-Davis will pay a dividend of 35 cents a share to stockholders of record April 12. The payment to more than 24,000 stockholders will exceed \$1,700,000.

The company has made a profit every year since 1876.

DR. BURLEW REJOINS SCHERING MEDICAL STAFF

Robert W. Burlew, M.D., returned to the Clinical Research Division of Schering Corporation, Bloomfield, N. J. pharmaceutical manufacturers, on February 1st after two years' service with the U. S. Army Medical Corps.

Dr. Burlew is a graduate of Duke University and of the University of Pennsylvania School of Medicine. He first joined the Schering medical staff in 1949.

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condition	incidence of liver dysfunction	incidence of blood lipid abnormalities	suggested therapy
obesity	frequent	frequent	Methischol plus balanced low calorie diet.
diabetes	frequent	frequent	Methischol as adjunct to diet. Insulin as necessary.
atherosclerosis	frequent	frequent	Methischol and high protein, low fat diet.
coronary disease	frequent	frequent	Methischol as adjunct to high protein, low fat diet and specific therapy.
alcoholism	frequent	frequent	Methischol plus high protein diet.

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...helps normalize liver function, increase phospholipid turnover, reduce fatty deposits, and stimulate regeneration of new liver cells...

...helps reduce elevated cholesterol levels and chylomicron ratios towards the normal, and aids in achieving normal fat metabolism.

new—higher B₁₂

the suggested daily therapeutic dose of 9 capsules or 3 tablespoonfuls of Methischol provides:

Choline Dihydrogen Citrate*	2.5 Gm.
dl, Methionine	1.0 Gm.
Inositol	0.75 Gm.
Vitamin B ₁₂	18 mcg.
Liver Concentrate and Desiccated Liver**	0.78 Gm.

*Present in syrup as 1.15 Gm. Choline Chloride
**Present in syrup as 1.2 Gm. Liver Concentrate

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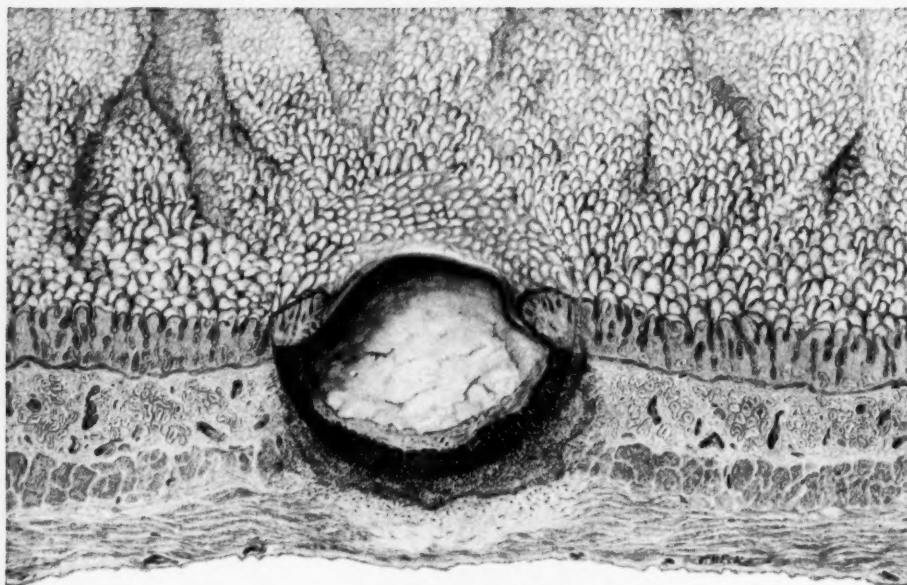
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Cross section of active duodenal ulcer.

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Pain of ulcer is associated with hypermotility; the pain is relieved when abnormal motility is controlled by Pro-Banthine.[®]

"In studying¹ the mechanism of ulcer pain, it is obvious that there are at least two factors which must be considered: namely, hydrochloric acid and motility.

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"Prompt relief of ulcer pain by ganglionic blocking agents... coincided exactly with cessation of abnormal motility and relaxation of the stomach."

Pro-Banthine (β -diisopropylaminoethyl xanthene-9-carboxylate methobromide, brand of propantheline bromide) is a new, improved, well tolerated anticholinergic agent which consistently reduces hypermotility of the stomach and intestinal tract. In peptic ulcer therapy² Pro-Banthine has brought about dramatic remissions, based on roentgenologic evidence. Concurrently there is a reduction of pain or, in many instances, the pain

and discomfort disappear early in the program of therapy.

One of the typical cases cited by the authors³ is that of a male patient who refused surgery despite the presence of a huge crater in the duodenal bulb.

"This ulcer crater was unusually large, yet on 30 mg. doses of Pro-Banthine [q.i.d.] his symptoms were relieved in 48 hours and a most dramatic diminution in the size of the crater was evident within 12 days."

Pro-Banthine is proving equally effective in the relief of hypermotility of the large and small bowel, certain forms of pylorospasm, pancreatitis and ureteral and bladder spasm. G. D. Searle & Co., Research in the Service of Medicine.

1. Ruffin, J. M.; Baylin, G. J.; Legerton, C. W., Jr., and Texter, E. C., Jr.: Mechanism of Pain in Peptic Ulcer, *Gastroenterology* 23:252 (Feb.) 1953.

2. Schwartz, I. R.; Lehman, E.; Ostrove, R., and Seibel, J. M.: A Clinical Evaluation of a New Anticholinergic Drug, Pro-Banthine, *Gastroenterology* 25:416 (Nov.) 1953.